

FIG. 1A
Nf1_{col2}^{-/-} Osteoblasts Secrete Increased Levels of Pyrophosphate (PP_i)

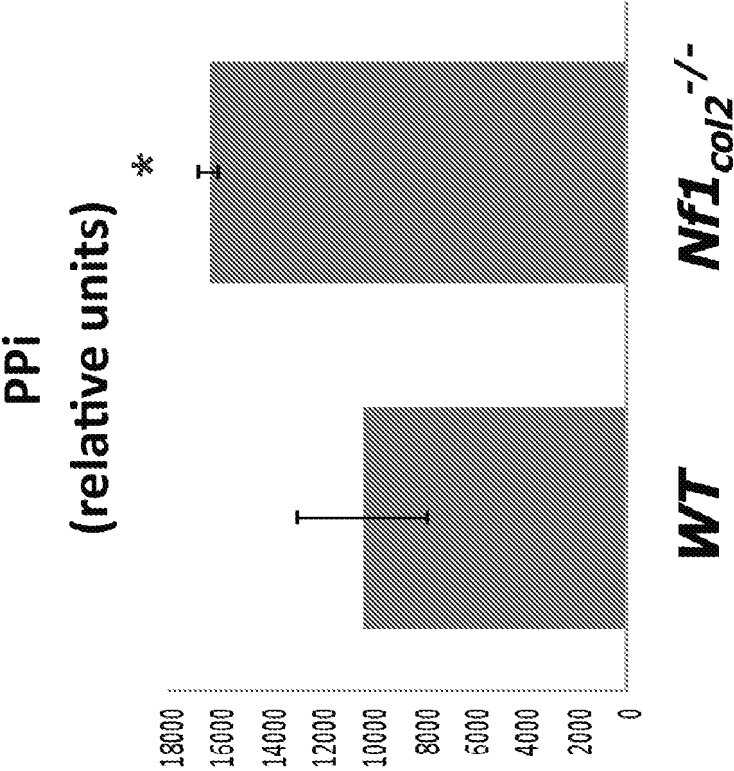


FIG. 1B
Increased *Ank* Expression in *Nf1*_{col2}^{-/-} Osteoblasts

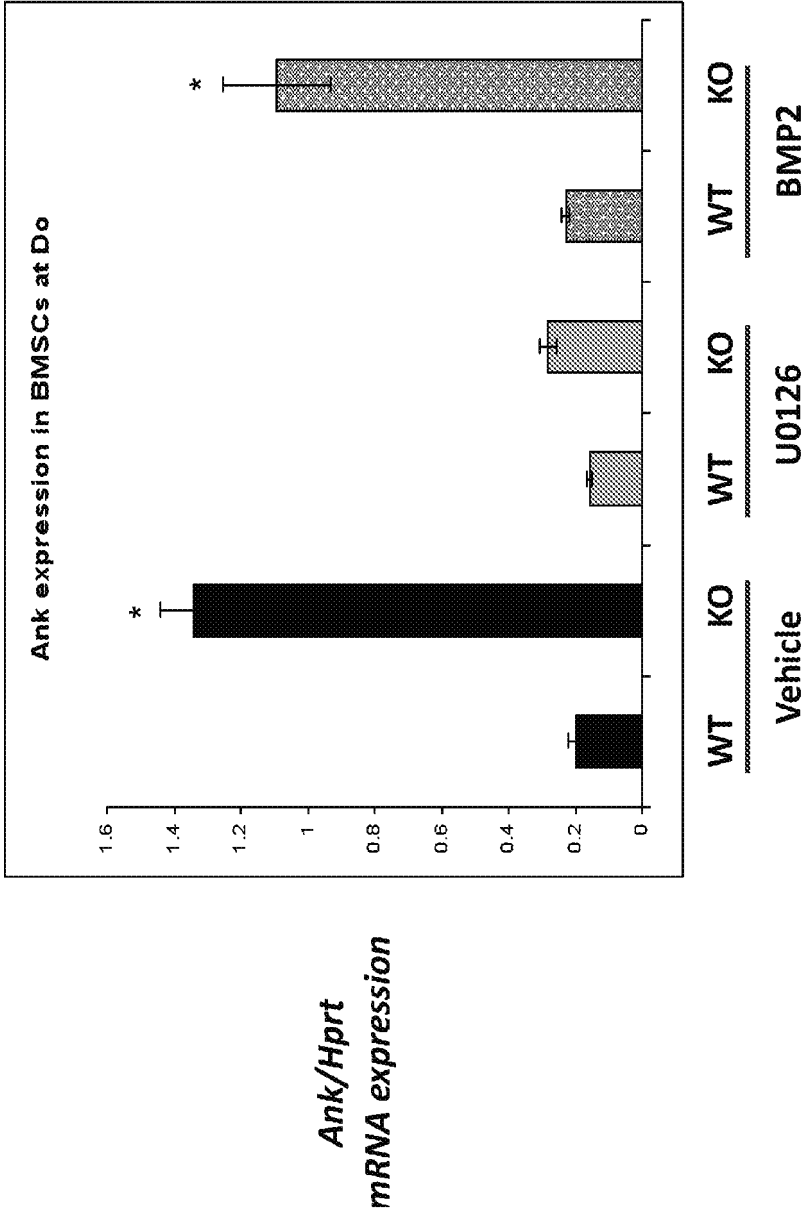
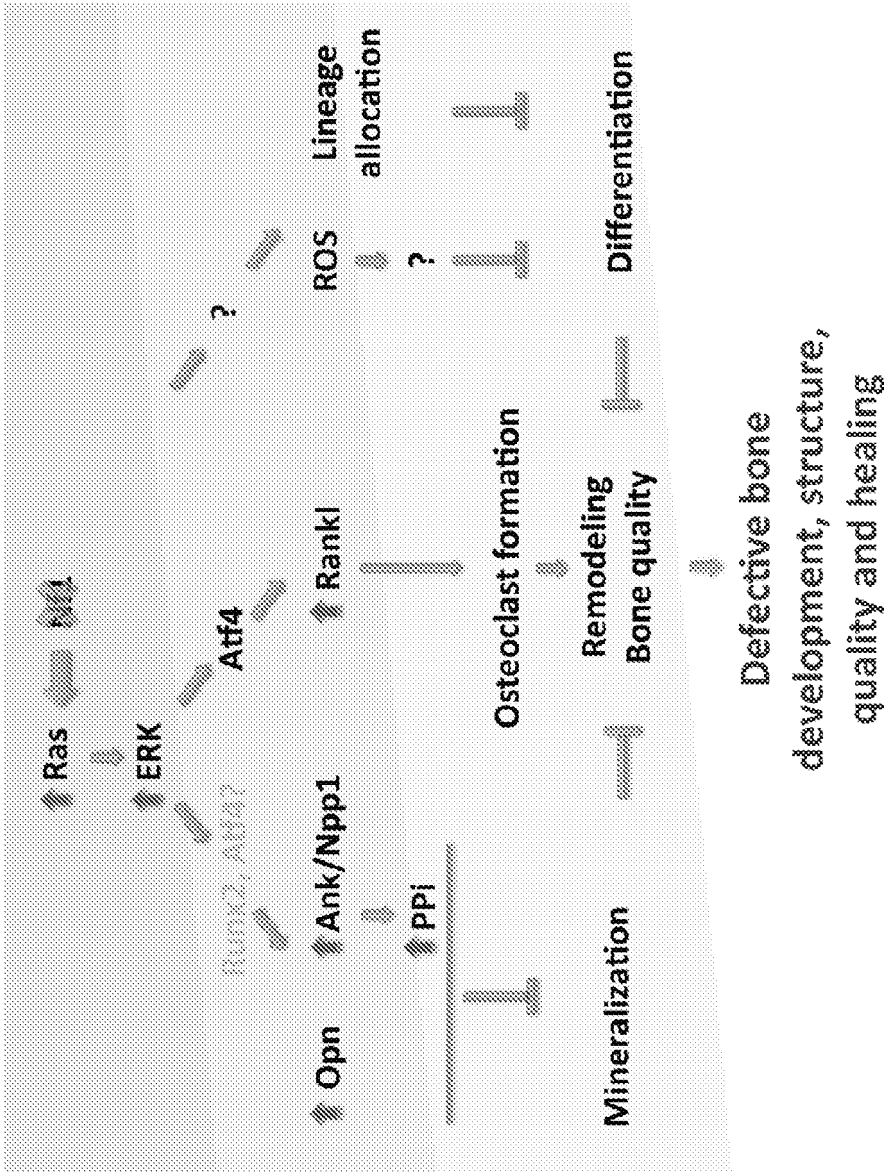


FIG. 2
Hypothetical Working Model for Defective Bone Matrix Mineralization in NF1_{col2}^{-/-} Mice



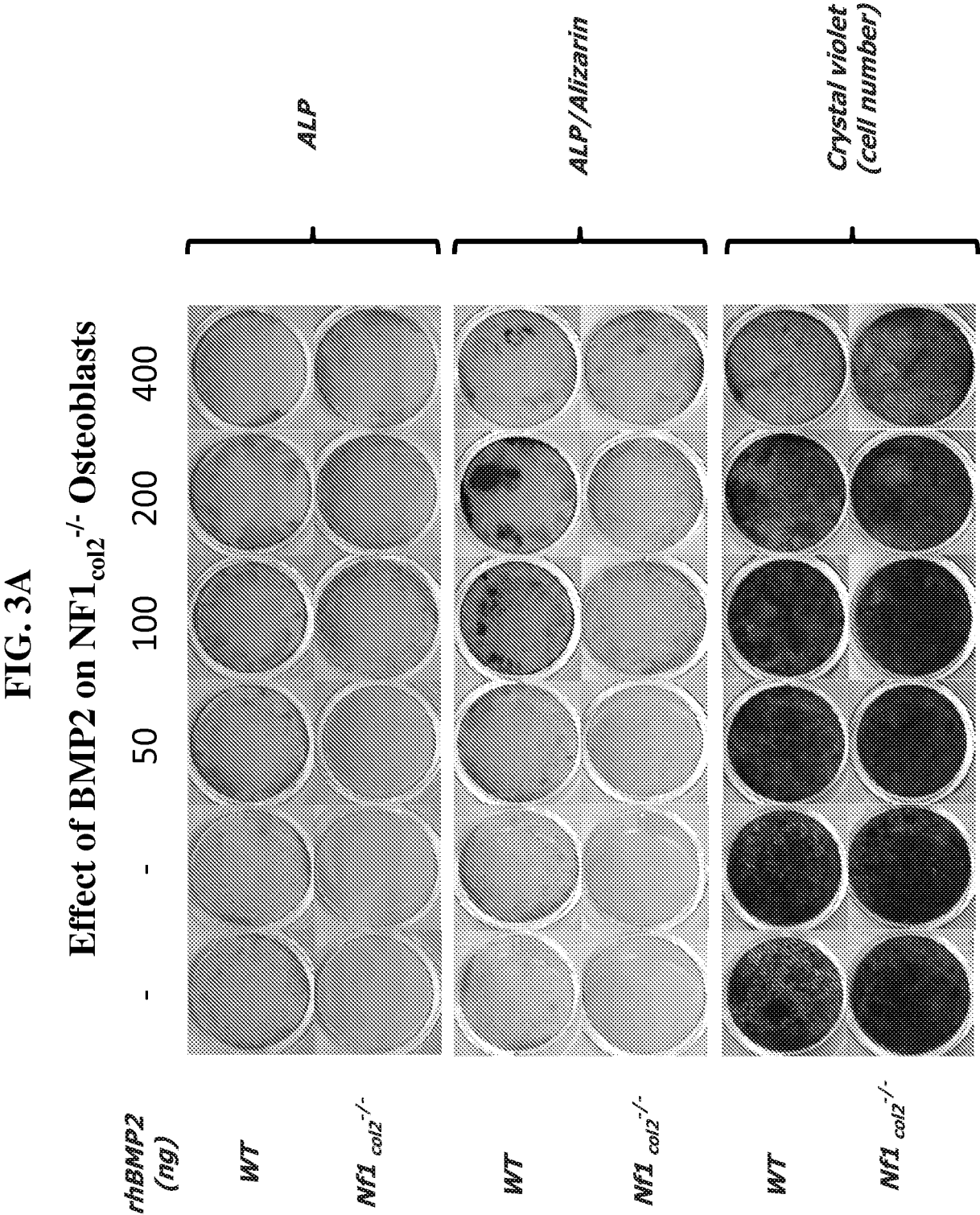


FIG. 3B

Effect of sTNALP-FcD₁₀ on Nf1^{col2}^{-/-} Bone Marrow Stromal Cells

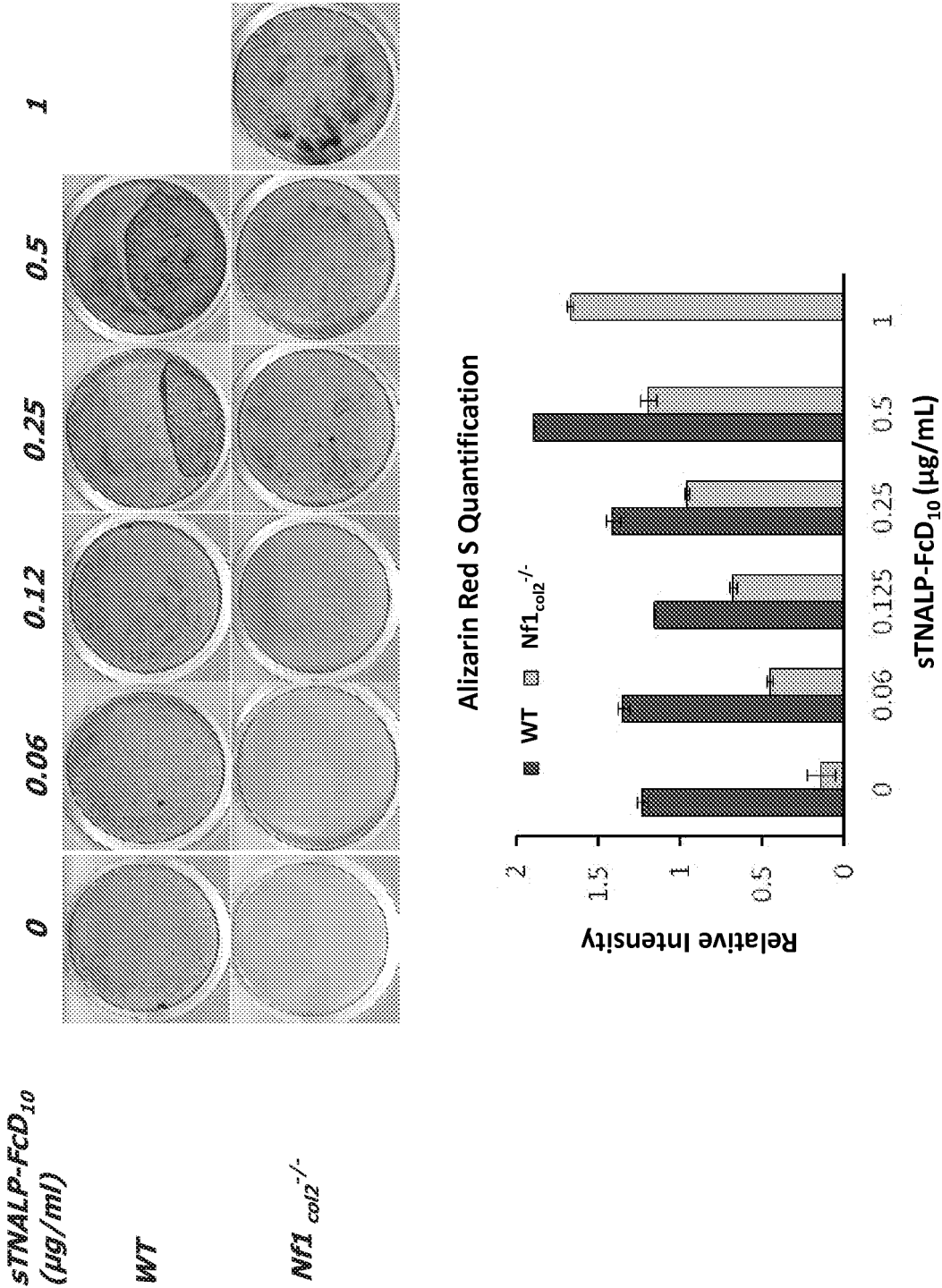


FIG. 3C
Effect of sTNALP-FcD₁₀ on NF1_{col2}^{-/-} Bone Marrow Stromal Cells

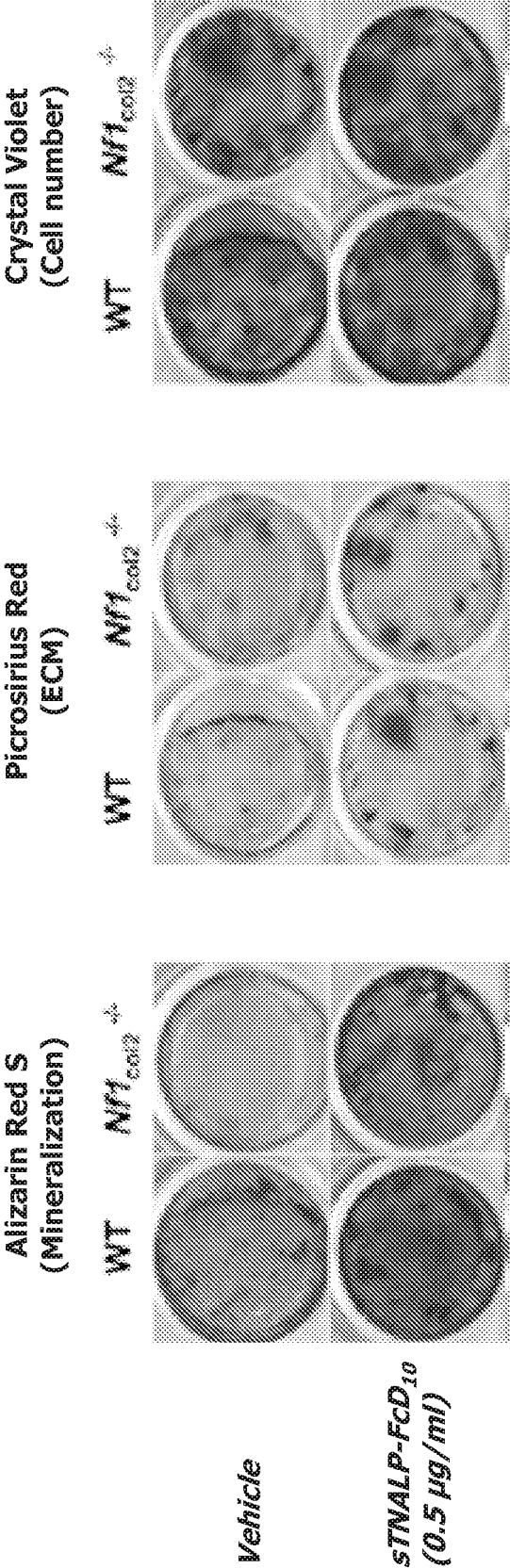


FIG. 3D
Effect of sTNALP-FcD₁₀ on Floxed NF1_{col2}^{-/-} Bone Marrow Stromal Cells

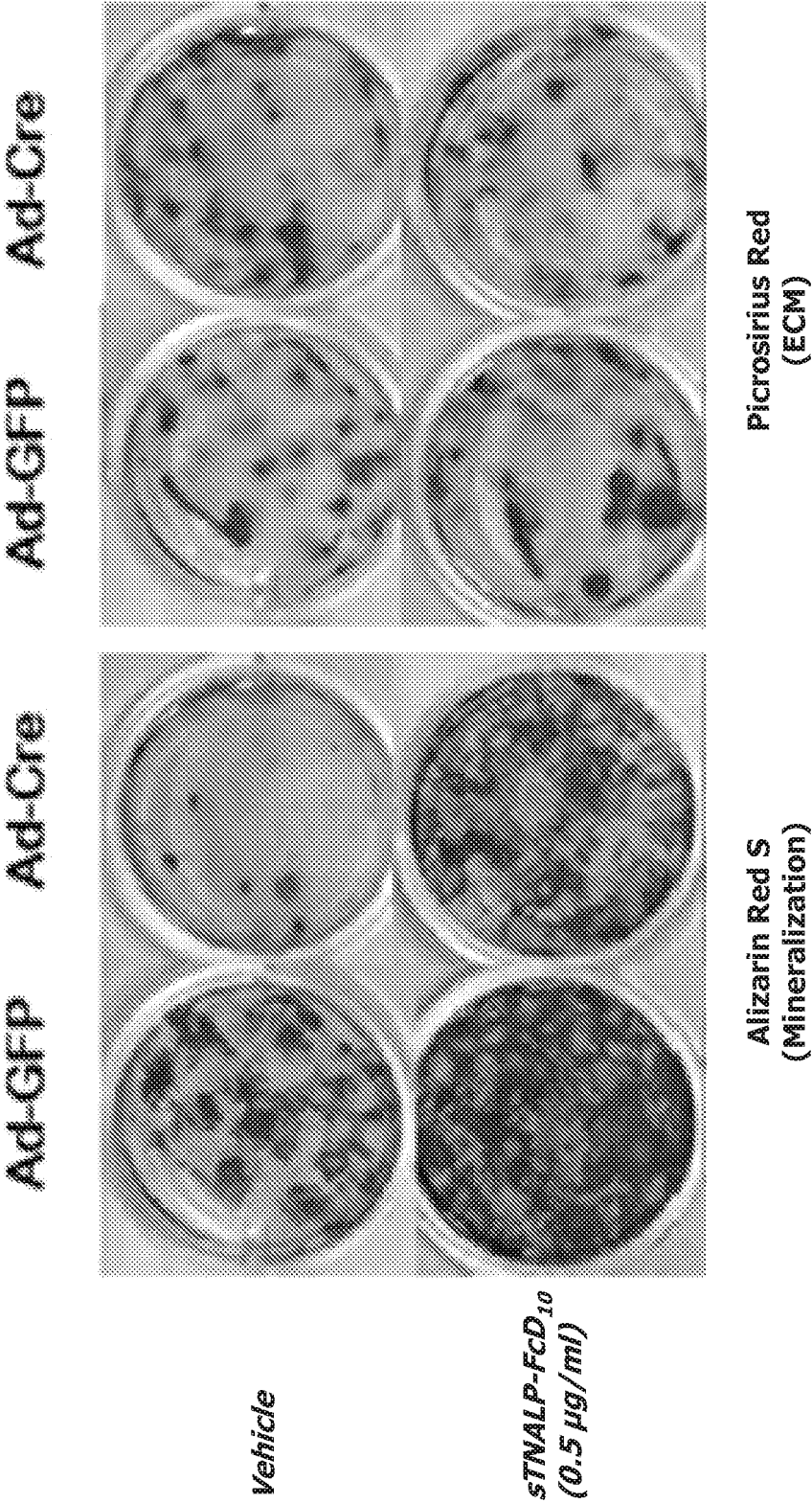


FIG. 3E
Effect of sTNALP-FcD₁₀ on Bone Volume in *Nf1_{col2}^{-/-}* Mice

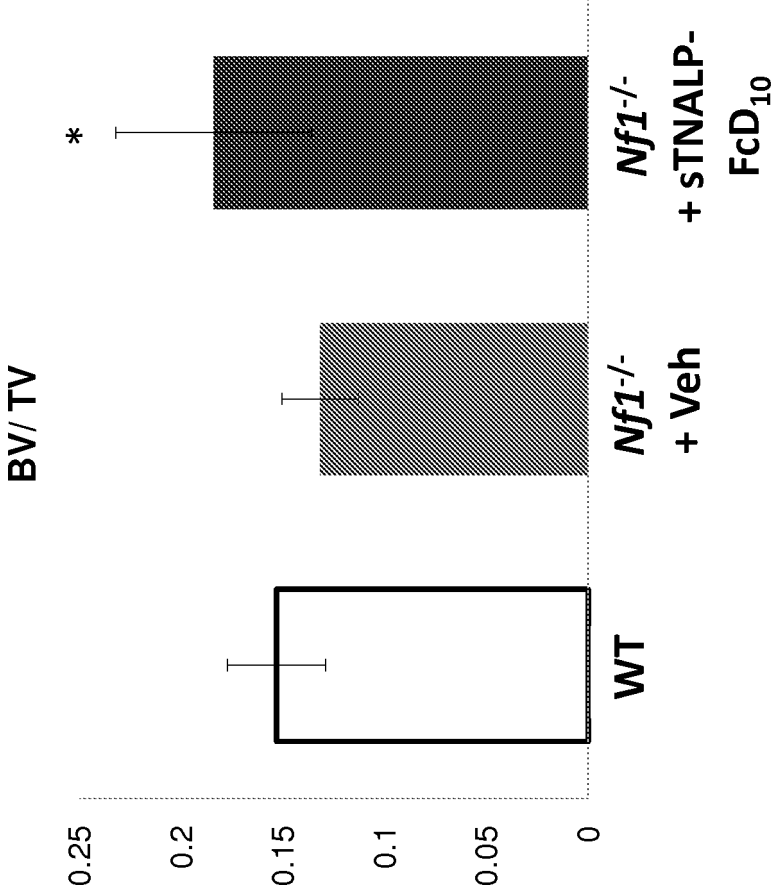
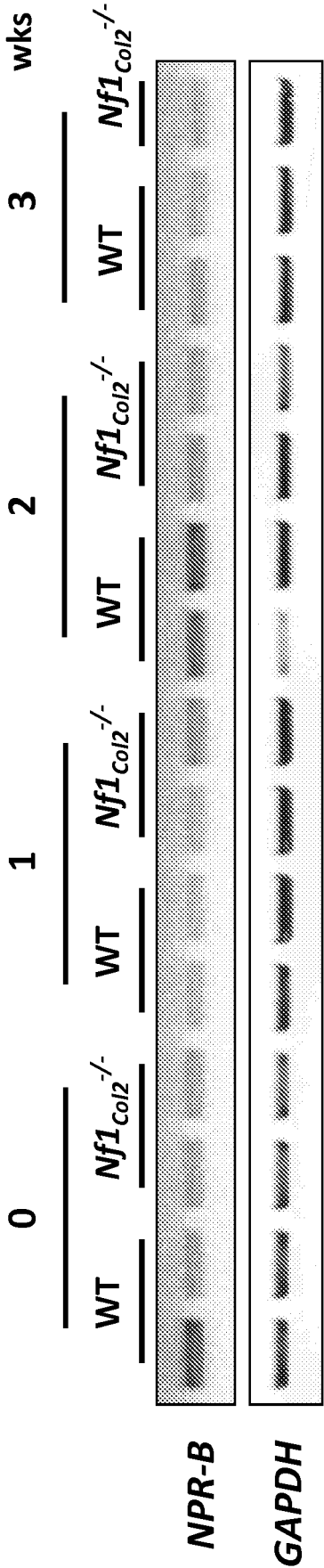
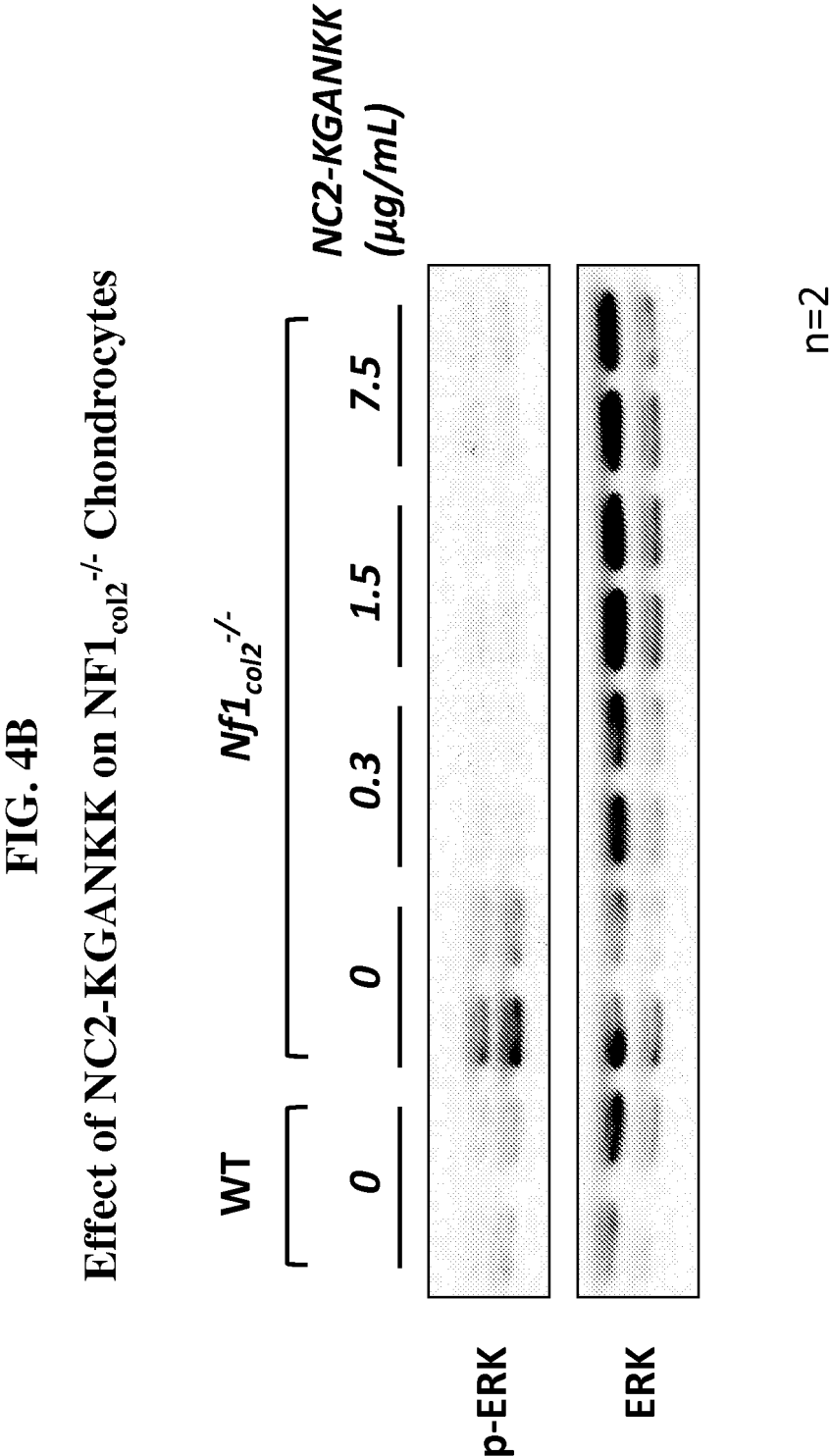


FIG. 4A
Expression of *NPR-B* Gene in *Nf1_{Col2}^{-/-}* Mice





P0 mice rib primary chondrocytes

FIG. 4C
Effect of NC2B on Naso-anal Length in $Nf1_{col2}^{-/-}$ Mice

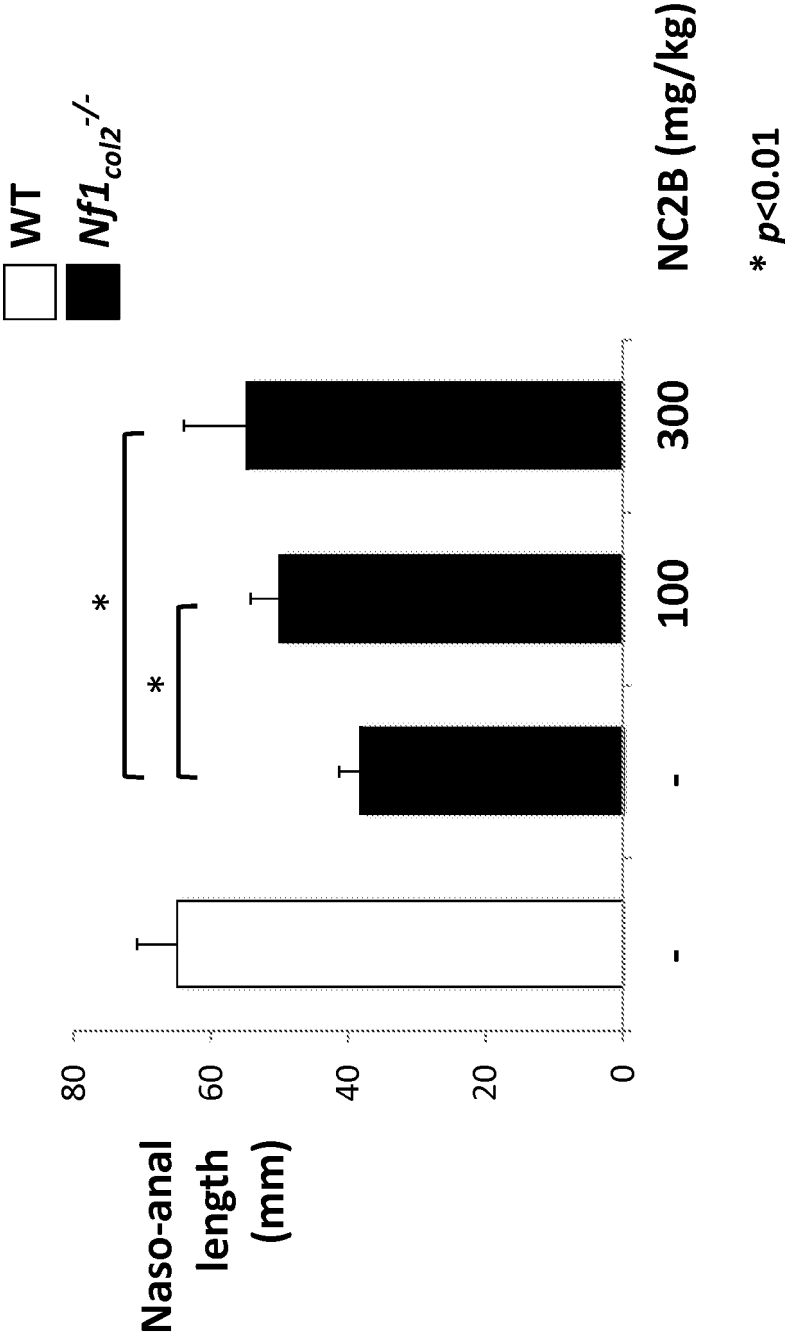


FIG. 4D
Effect of NC2B on Tibia Length in $Nf1_{col2}^{-/-}$ Mice

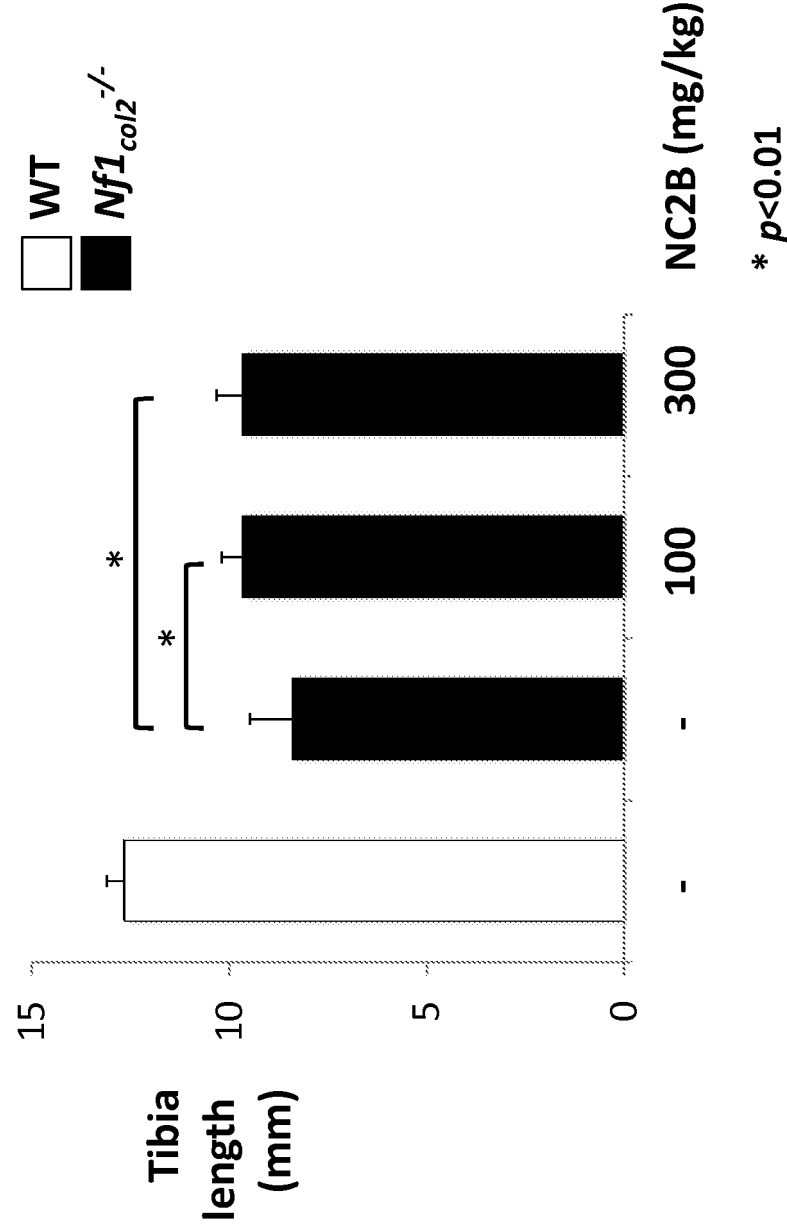


FIG. 4E
Effect of NC2B on Growth Plates in $Nf1_{col2}^{-/-}$ Mice

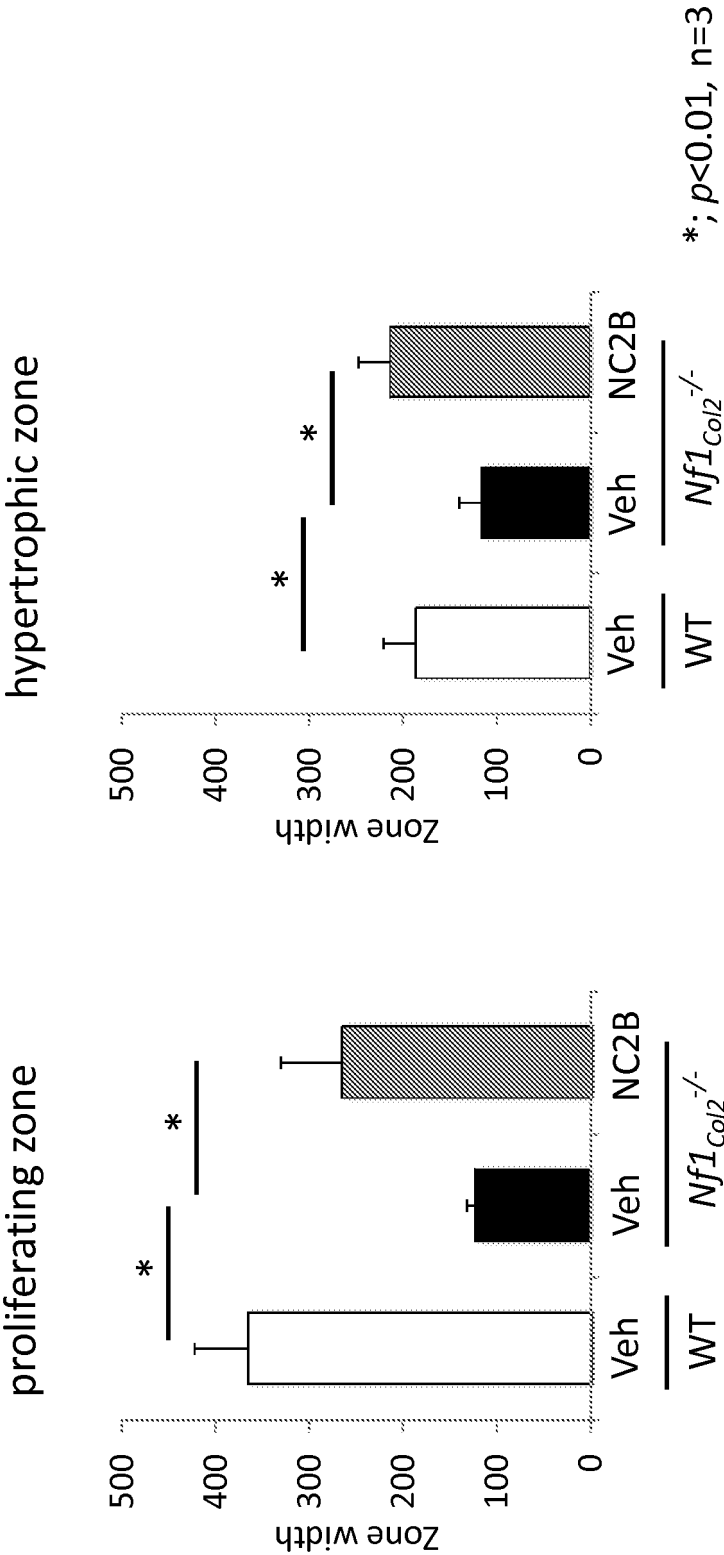


FIG. 5A
Schematic Structure of TNALP and hsTNALP-FcD₁₀
(With and Without Signal Sequence)

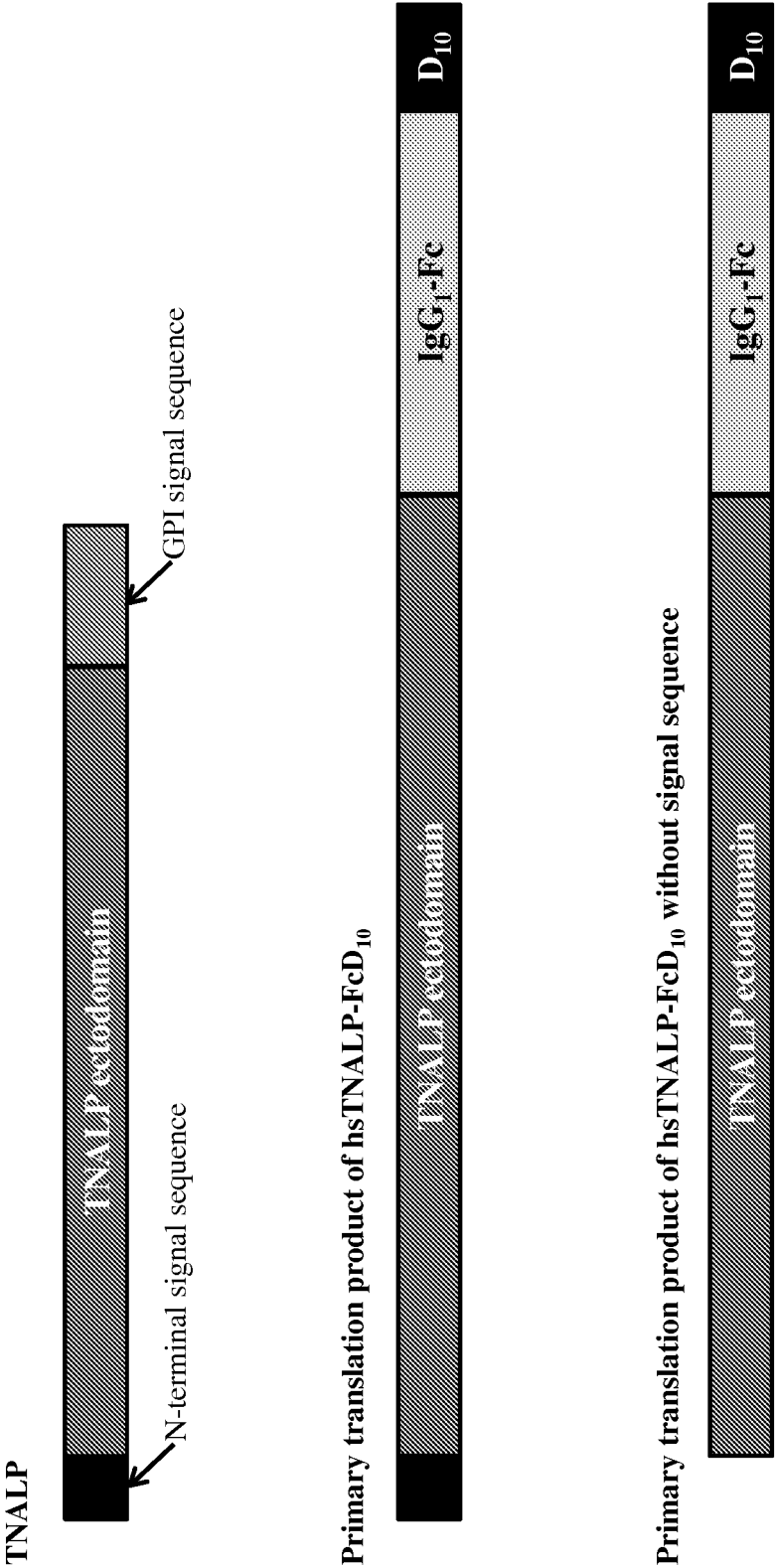


FIG. 5B
hsTNALP-FcD₁₀ Protein Sequence
(With and Without Signal Sequence)

sTNALP-FcD ₁₀ (w/sig. seq.)	MVSPFLVLAIGTCLTNSLVPEKEKDPKYWRDQAQETLKYLELQKLNTNVAKNVIMFLGDMGVSTVTAA RILKGQLHHNPGEETRLEMDKFFVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCN TTQGNEVTSILRWAKDAGKSVGIVTTTRVNHA TPSAAYAH SADRWDYSDNEMPPEALSQGCKDIA YQLMH NIRDIDVIMGGGRKYMYPKNKTDVEYESDEKARGTRLDGLDLVDTWKSFKPRYKHSHF IWNRTELLTLDP HNVDYLLGLFEFGDMQYELNRNNVTDPSLSEMVVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALH EAVEMDRAIGQAAGSLTSSEDTLTVVTADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYGNPGP YKVVGGERENVSMVDYAHNNYQAQSAVPLRHETHGGEDVAVFSKGPMAHLLHGVHEQNYVPHVMAYAACT GANLGHCAPASSLLKDKTHTCPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFFLYSKLTVDKSR WQQGNVFSSCSVMHEALHNHYTQKSLSLSPGKDIDDDDDDDDDD (SEQ ID NO: 1201)
sTNALP-FcD ₁₀ (w/o sig. seq.)	LVPEKEKDPKYWRDQAQETLKYLELQKLNTNVAKNVIMFLGDMGVSTVTAARILKGQLHHNPGEETRL EMDKFFPVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCNTTQGNEVTSILRWAKDA GKSVGIVTTTRVNHA TPSAAYAH SADRWDYSDNEMPPEALSQGCKDIA YQLMHNIRDIDVIMGGGRKMY PKNKTDVEYESDEKARGTRLDGLDLVDTWKSFKPRYKHSHF IWNRTELLTLDPPHNVDYLLGLFEFGDMQY ELNRNNVTDPSLSEMVVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALHEAVEMDRAIGQAAGSLT SEDTLTVVTADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYGNPGPYKVVGGERENVSMVDYA HNNYQAQSAVPLRHETHGGEDVAVFSKGPMAHLLHGVHEQNYVPHVMAYAACTIGANLGHCAPASSLLKDKT HTCPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQV SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFFLYSKLTVDKSRWQQGNVFSSCSVMHEALH NHYTQKSLSLSPGKDIDDDDDDDDDD (SEQ ID NO: 1204)

FIG. 5C

hsTNALP-Fc Protein Sequence
(With and Without Signal Sequence)

sTNALP-Fc (w/sig. seq.)	MVSPFLVLAIGTCLTNSLVPEKEKDPKYWRDQAQETLKYALELQKLTNTNVAKNVIMFLGDMGVSTVTAA RILKGQLHHNPGEETRLEMDKFFPVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCN TTQGNEVTSILRWAKDAGKSVGIVTTTRVNHA TPSAAYAHSA DRDWYSDNEMPPEALSQGCKDIA YQLMH NIRDIDVIMGGGRKYMYPKNKTDVEYESDEKARGTRLDGLDLDVTWKSFKPRYKXSHFIWNRTELLTLDP HNVDYLLGLFEFGDMQYELNRNNVTDPSLSEMVVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALH EAVEMDRAIGQA GSLTSSEDITLVVTADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYGNPGP YKVVGGERENVSMVDYAHNNYQAQSAVPLRHETHGGEDVAVFSKGPM AHLHLHG VHEQNYVPHVMAYAACT GANLGHCAPASSLKDKTHTCPPCPAPELLGGPSVFLFPKPKDITLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 1220)
sTNALP-Fc (w/o sig. seq.)	LVPEKEKDPKYWRDQAQETLKYALELQKLTNTNVAKNVIMFLGDMGVSTVTAA RILKGQLHHNPGEETRL EMDKFFPVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCNTTQGNEVTSILRWAKDA GKSVGIVTTTRVNHA TPSAAYAHSA DRDWYSDNEMPPEALSQGCKDIA YQLMHNIRDIDVIMGGGRKMY PKNKTDVEYESDEKARGTRLDGLDLDVTWKSFKPRYKXSHFIWNRTELLTLDPHNVVDYLLGLFEFGDMQY ELNRNNVTDPSLSEMVVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALHEAVEMDRAIGQA GSLTS SEDTLVVTADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYGNPGPYKVVGGERENVSMVDYA HNNYQAQSAVPLRHETHGGEDVAVFSKGPM AHLHLHG VHEQNYVPHVMAYAACTIGANLGHCAPASSLKDKT HTCPPCPAPELLGGPSVFLFPKPKDITLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQV SLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPGK (SEQ ID NO: 1221)

FIG. 5D

hsTNALP-FcD₁₀ DNA Sequence

atgggtttcac cattcttagt actggccatt ggcacctgcc ttactaactc cttagtgcca gagaaagaga aagacccccaa gtactggcga
 gaccaagcgc aagagacact gaaatatgcc ctggagcttc agaagctcaa caccacactg gctaaaatg tcatcatgtt cctgggagat
 gggatgggtg tctccacagt gacggtgcc cgcacctca aggtcagct ccaccacaac cctggggagg agaccaggct ggagatggac
 aagttcccc tegtggccct ctccaagacg tacaacacca atgcccagggt cctgacagc gccggcaccg ccaccgccta cctgtgtggg
 gtgaaggcca atgagggcac cgtggggta agcgcagcca ctgagcgttc ccggtgcaac accaccagg ggaacgaggt cacctccatc
 ctgcgtggg ccaaggacgc tgggaaatct gtggcattg tgaccaccac gagagtgaac catgccacc catcgccgc ctacgcccac
 tcggctgacc gggactggtg ctacagacaac gagatgcccc ctgaggcctt gagccaggc tgtaaggaca tgcctacca gctcatgcat
 aacatcaggg acattgacgt gatcatggg ggtggccgga aatacatgta cccaagaat aaaactgatg tggagtatga gagtgcagag
 aaagccaggg gcacgaggct ggacggcctg gacctcgtt acacctggaa gagcttcaaa ccgagatata agcactccca ctcatctgg
 aacgcacgg aactcctgac ccttgacccc cacaatgtgg actacctatt ggtctcttc gagccagggt acatgcagta cgagctgaac
 aggaacaacg tgacggaccc gtcactctcc gagatggtgg tggtggccat ccagatcctg cggaagaacc ccaaaggctt ctcttgctg
 gtggaaggag gcagaattga ccacgggcac catgaaggaa aagccaagca ggccctgcat gaggcgttg agatggaccg ggccatcggg
 caggcaggca gcttgacctc ctcggaagac actctgaccg tggtcactgc ggaccattcc cactcttca catttggtgg atacacccc
 cgtggcaact ctatctttgg tctggcccc atgctgagt acacagaaa gaagcccttc actgccatcc tgatggcaa tgggcctggc
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 cacgagaccc acggcgggga ggaactggcc gtcttctca agggcccat ggcgacctg ctgcacggcg tccacgagca gaactacgtc
 cccacagtga tggcgtatgc agcctgcac ggggccaacc tcggccactg tgctcctgcc agctcgtTA AGgacaaaac tcacacatgc
 ccacogtgc cagcacctga actcctgggg ggaactcag tcttctctt cccccaaaa cccaaggaca cctcatgat ctcccgacc
 cctgaggtca catgctggt ggtggactg agccacgaag accctgaggt caagttcaac tggtaactgg acggcgtgga ggtgcataat
 gccaaagaca agccgcggga ggagcagtac aacagcacgt accgtgtggt cagcgtctc cagcgtctgc accaggactg gctgaatggc
 aaggagtaca agtgcaaggt ctccaacaaa gccctccag ccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca
 caggtgtaca cctggcccc atccccggag gagatgacca agaaccaggt cagcctgacc cagcctgcca aaggttcta tcccagcagc
 atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cagcctccc gtgtgact ccgacggctc ctcttctc
 tatagcaagc tcaccgtgga caagagcagg tggcagcagg ggaactctt ctcatgctcc gtgatgcatg aggtctctgca caaccactac
 acgcagaaga gcctctccct gtctccgggt aaagATATCG ATGACGATGA CGATGACGAT GACGATGACT AG (SEQ ID NO: 1217)

FIG. 6
Human Soluble Tissue Nonspecific Alkaline Phosphatase
(hsTNALP) Protein Sequence

hsTNALP (1-502)	<u>MVSPFLVLAIGTCLTNSL</u> VPKEKDPKYWRDQAQETLK YALELQKLNTN VAKNVI IMFLGD GMGVSTVTAARI LK QQLHHNP GEE TRLEMDKFPF VALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCNTTQG NEVTSILRWAKDAGKSVGIVTTTRVNHATPSAA YAH SADRDWYSDNEMPPEALSQGCKDIA YQLMHN IRDID VIMGGGRKYMYPKNKTDVEYESDEKARGTRLDGLDLVDTWKSFKPRYKHSHF IWNRT ELLTLD PHNV DYLLG LFE PGDMQYELNR NNVTDP SLSEM VVVAIQILRKNPKGFFLLVEGGRIDHGHHEGKAKQALHEAVEMDRAIG QAGSLTSS EDTLTV VIADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYNGNGPGYKVVGGGERENV MVDYAHNNYQAQSAVPLRHETHGGEDVAVFSKGPMAHLLHGVHEQNYVPHVMAYAAACIGANLGHCAPASS (SEQ ID NO: 1202)
hsTNALP (18-502)	LVPEKEKDPKYWRDQAQETLK YALELQKLNTN VAKNVI IMFLGD GMGVSTVTAARILK QQLHHNP GEE TRLEM DKFPFVALSKTYNTNAQVPDSAGTATAYLCGVKANEGTVGVSAATERSRCNTTQ NEVTSIL RWAKDAGKSV GIVTTTRVNHATPSAA YAH SADRDWYSDNEMPPEALSQGCKDIA YQLMHN IRDIDVIMGGGRKYMYPKNKTD VEYESDEKARGTRLDGLDLVDTWKSFKPRYKHSHF IWNRT ELLTLD PHNV DYLLG FE PGDMQYELNR NNVT DPSLSEM VVVAIQILRKNPKGFFLL VEGGRIDHGHHEGKAKQALHEAVEMDRAIGQAGSLTSS EDTLTV VI ADHSHVFTFGGYTPRGNSIFGLAPMLSDTDKKPFTAILYNGNGPGYKVVGGGERENVSMVDYAHNNYQAQSAVPL RHETHGGEDVAVFSKGPMAHLLHGVHEQNYVPHVMAYAAACIGANLGHCAPASS (SEQ ID NO: 1205)

FIG. 7
Exemplary Fc Sequence (IgG-1)

DKTHTCPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV
HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV
YTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSGFFLYSKLTV
DKSRWQQGNVFSQSVMEALHNHYTQKSLSLSPGK (SEQ ID NO: 401)

FIG. 8
Multiple Sequence Alignment of Tissue Nonspecific Alkaline Phosphatase (TNALP)

FIG. 8 (cont'd)

181	P09487 PPBT_BOVIN	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMY	NIKDIEVIMG	GGRKYMFPKN	RTDVEYELDE
	Q29486 PPBT_FELCA	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMH	NVRDIEVIMG	GGRKYMFPKN	RTDVEYEMDE
	P05186 PPBT_HUMAN	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMH	NIRDIDVIMG	GGRKYMFPKN	KTDVEYESDE
	P09242 PPBT_MOUSE	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMH	NIKDIDVIMG	GGRKYMFPKN	RTDVEYELDE
	P08289 PPBT_RAT	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMH	NIKDIDVIMG	GGRKYMFPKN	RTDVEYELDE
	Q9N0V0 Q9N0V0_CANFA	SADRDWYSDN	EMPPEALSQG	CKDIAYQLMH	NVKDIEVIMG	GGRKYMFPKN	RTDVEYEMDE
	Consensus	*****	*****	*****	*:****	*****:***	:***** **
		SADRDWYSDN	EMPPEALSQG	CKDIAYQLMX	NXXDIXVIMG	GGRKYMFPKN	XTDVEYEXDE
241	P09487 PPBT_BOVIN	KARGTRLDGL	NLIDIWKSFK	PKHKHSHYVW	NRTDLLALDP	HSVDYLLGLF	EPGDMQYELN
	Q29486 PPBT_FELCA	KARGTRLDGL	NLVDIWKSFK	PRHKHSHYVW	NRTELLTLDP	YGVDYLLGLF	EPGDMQYELN
	P05186 PPBT_HUMAN	KARGTRLDGL	DLVDTWKSFK	PRYKHSFIW	NRTELLTLDP	HNVDYLLGLF	EPGDMQYELN
	P09242 PPBT_MOUSE	KARGTRLDGL	DLISIWKSFK	PRHKHSHYVW	NRTELLALDP	SRVDYLLGLF	EPGDMQYELN
	P08289 PPBT_RAT	KARGTRLDGL	DLISIWKSFK	PRHKHSHYVW	NRTELLALDP	SRVDYLLGLF	EPGDMQYELN
	Q9N0V0 Q9N0V0_CANFA	KSTGARLDGL	NLIDIWKNFK	PRHKHSHYVW	NRTELLALDP	YFVDYLLGLF	DPGDMQYELN
	Consensus	*:*****	:*:. **.*	*:*****:*	***:***	*****	:*****
		KXXGXRLDGL	XLXXXWXXFK	PXXKHSXXW	NRTXLLXLDP	XXVDYLLGLF	XPGDMQYELN
301	P09487 PPBT_BOVIN	RNNATDPSLS	EMVEMAIRIL	NKNPKGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDQAIG
	Q29486 PPBT_FELCA	RNSTTDPSLS	EMVEIAIKIL	SKNPKGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDQAIG
	P05186 PPBT_HUMAN	RNNVTDPSLS	EMVVAIQIL	RKNPKGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDRAIG
	P09242 PPBT_MOUSE	RNNLTDPSLS	EMVEVALRIL	TKNLKGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDQAIG
	P08289 PPBT_RAT	RNNLTDPSLS	EMVEVALRIL	TKNPKGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDEAIG
	Q9N0V0 Q9N0V0_CANFA	RNNVTDPSLS	EMVEIAIKIL	SKKPRGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDRAIG
	Consensus	** *****	***:***	*:*****	*****	*****	:*****
		RNXXTDPSLS	EMVXXAXXIL	XXXXGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDXAIG

FIG. 8 (cont'd)

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361  P09487|PPBT_BOVIN      TLTVVTADHS  HVFTFGGYTP  RGNSTFGLAP  MVSDTDKKPF  TAILYGNQPG
    Q29486|PPBT_FELCA      TLTIVTADHS  HVFTFGGYTP  RGNSTFGLAP  MVSDTDKKPF  TSILYGNQPG
    P05186|PPBT_HUMAN      TLTVVTADHS  HVFTFGGYTP  RGNSTFGLAP  MLSDTDKKPF  TAILYGNQPG
    P09242|PPBT_MOUSE      TLTVVTADHS  HVFTFGGYTP  RGNSTFGLAP  MVSDTDKKPF  TAILYGNQPG
    P08289|PPBT_RAT        TLTVVTADHS  HVFTFGGYTP  RGNSTFGLAP  MVSDTDKKPF  TAILYGNQPG
    Q9N0V0|Q9N0V0_CANFA    TLTVVTADHS  HVFTFGGYTP  RGNSTFGLAP  MVSDTDKKPF  TAILYGNQPG
    Consensus              :*: ** ; * :***:***** *:***** **:*****
421  XAGXTSXXD  TLTXTADHS  HVFTFGGYTP  RGNSTFGLAP  MXSDTDKKPF  TXILYGNQPG

    YKVVGGEREN  VSMVDYAHNN  YQAQSAVPLR  HETHGGEDVA  VFAKGPM AHL  LHGVQEQNYI
    YKVVGGEREN  VSMVDYAHNN  YQAQSAVPLR  HETHGGEDVA  VFAKGPM AHL  LHGVHEQNYI
    YKVVGGEREN  VSMVDYAHNN  YQAQSAVPLR  HETHGGEDVA  VESKGPMAHL  LHGVHEQNYV
    YKVVDGEREN  VSMVDYAHNN  YQAQSAVPLR  HETHGGEDVA  VFAKGPM AHL  LHGVHEQNYI
    YKVVDGEREN  VSMVDYAHNN  YQAQSAVPLR  HETHGGEDVA  VFAKGPM AHL  LHGVHEQNYI
    YKVVGGEREN  VSMVDYAHNN  YQAQSAVPLR  HETHGGEDVA  VFAKGPM AHL  LHGVHEQNYI
    ****.***** ***** ***** **;***** *****;****;
    YKVVGGEREN  VSMVDYAHNN  YQAQSAVPLR  HETHGGEDVA  VFXKGPMAHL  LHGVXEQNYX

481  PHVMAYAACI  GANRDHCASA  SSSGSPSPGP  LLLLLALPL  GSLF(SEQ  ID NO: 1206)
    PHVMAYAACI  GANLDHCASA  SSAGSPSPGP  LFLLLALPSL  GILF(SEQ  ID NO: 1207)
    PHVMAYAACI  GANLGHCAFA  SSAGSLAAGP  LLLALALYPL  SVLF(SEQ  ID NO: 1208)
    PHVMAYASCI  GANLDHCAWA  GSGSAPSPGA  LLLPLAVLSL  PTLF(SEQ  ID NO: 1209)
    PHVMAYASCI  GANLDHCAWA  SSASSPSPGA  LLLPLALFPL  RPLF(SEQ  ID NO: 1210)
    PHVMAYAACI  GANQDHCASA  SSAGGSPSPGP  LLLLLALFV  GILF(SEQ  ID NO: 1211)
    *****; ** * * * * * * * * * * * * * * * *
    PHVMAYAXCI  GANXXHCAXA  XSXXXXXXGX  LXLXLA XXXX  XLFL(SEQ  ID NO: 1216)

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FIG. 9

Multiple Sequence Alignment of Alkaline Phosphatase
(TNALP, GALP, PLALP, and IALP)

CLUSTAL 2.0.5 multiple sequence alignment									
TNALPrn	MILP-----F	LVLAIGTCLT	NSFVPEKEKD	PSYWRQQAQE	TKNALKLQK	LNTNVAKNII	55		
TNALPmm	MISP-----F	LVLAIGTCLT	NSFVPEKERD	PSYWRQQAQE	TKNALKLQK	LNTNVAKNVI	55		
TNALPhs	MISP-----F	LVLAIGTCLT	NSLVPEKEKD	PKYWRDQAQE	TKYALELQK	LNTNVAKNVI	55		
TNALPcf	-----	-----	-----EKD	PKYWRDQAQQ	TKYALRLQN	LNTNVAKNVI	33		
TNALPfc	MISP-----F	LVLAIGTCLT	NSLVPEKEKD	PKYWRDQAQQ	TKNALRLQK	LNTNVVKNVI	55		
TNALPbt	MISP-----F	LLLAIGTCFA	SSLVPEKEKD	PKYWRDQAQQ	TKNALRLQT	LNTNVAKNVI	55		
GALPhs	MQGPWV---L	LLGLRLQLS	LGIIPVEEEN	PDFWNRQAAE	ALGAAKKLQP	AQT-AAKNLI	56		
PLALPhs	MLGPCMLLLL	LLGLRLQLS	LGIIPVEEEN	PDFWNRQAAE	ALGAAKKLQP	AQT-AAKNLI	59		
IALPhs	MQGPWV---L	LLGLRLQLS	LGVTPAFEEEN	PAFWNRQAAE	ALDAAKKLQP	IQK-VAKNLI	56		
Consensus	XXXXXXXXXX	XXXXXXXXXX	*.: * :*. :* : * :* :*	XXXXXXXAXX	XXXXXXXXLQX	XXXXXXXXKXI			
TNALPrn	MFLGDGMGVS	TVTAARILKG	QLHNTGEET	RLEMDKFPFV	ALSKTYNTNA	QVPDSAGTAT	115		
TNALPmm	MFLGDGMGVS	TVTAARILKG	QLHNTGEET	RLEMDKFPFV	ALSKTYNTNA	QVPDSAGTAT	115		
TNALPhs	MFLGDGMGVS	TVTAARILKG	QLHNPGEET	RLEMDKFPFV	ALSKTYNTNA	QVPDSAGTAT	115		
TNALPcf	MFLGDGMGVS	TVTATRILKG	QLHNPGEET	RLEMDKFPYV	ALSKTYNTNA	QVPDSAGTAT	93		
TNALPfc	MFLGDGMGVS	TVTAARILKG	QLHNPGEET	RLEMDKFPYV	ALSKTYNTNA	QVPDSAGTAT	115		
TNALPbt	MFLGDGMGVS	TVTAARILKG	QLHSPGEET	KLEMDKFPYV	ALSKTYNTNA	QVPDSAGTAT	115		
GALPhs	IFLGDGMGVS	TVTAARILKG	QKDKLGPET	FLAMDRFPYV	ALSKTYSVDK	HVPDSGATAT	116		
PLALPhs	IFLGDGMGVS	TVTAARILKG	QKDKLGPEI	PLAMDRFPYV	ALSKTYNVDR	HVPDSGATAT	119		
IALPhs	LFLGDGLGVP	TVTATRILKG	QKNGKLGPEI	PLAMDRFPYL	ALSKTYNVDR	QVPDSAAATAT	116		
Consensus	:*****:***	*****:*****	* :. * *	* **::***: *	*****:***	:*****:***			
	XFLGDGXGVX	TVTAXRILKG	QXXXXXXGXEX	XLXMDXFPXX	ALSKTYXXXXX	XVPDSXXTAT			

FIG. 9 (cont'd)

TNALPrn	AYLCGVKANE	GTGVSAATE	RTRCNTTQGN	EVTSILRWAK	DAGKSVGIVT	TTRVNHATPS	175
TNALPmm	AYLCGVKANE	GTGVSAATE	RTRCNTTQGN	EVTSILRWAK	DAGKSVGIVT	TTRVNHATPS	175
TNALPhs	AYLCGVKANE	GTGVSAATE	RSRCNTTQGN	EVTSILRWAK	DAGKSVGIVT	TTRVNHATPS	175
TNALPcf	AYLCGVKANE	GTGVSAATQ	RTHCNTTQGN	EVTSILRWAK	DAGKSVGIVT	TTRVNHATPS	153
TNALPfc	AYLCGVKANE	GTGVSAATQ	RTQCNTTQGN	EVTSILRWAK	DSGKSVGIVT	TTRVNHATPS	175
TNALPbt	AYLCGVKANE	GTGVSAATQ	RSQCNTTQGN	EVTSILRWAK	DAGKSVGIVT	TTRVNHATPS	175
GALPhs	AYLCGVKGNF	QTIGLSAAAR	FNQCNTTRGN	EVISVMNRK	KAGKSVGVVT	TTRVQHASP	176
PLALPhs	AYLCGVKGNF	QTIGLSAAAR	FNQCNTTRGN	EVISVMNRK	KAGKSVGVVT	TTRVQHASP	179
IALPhs	AYLCGVKANF	QTIGLSAAAR	FNQCNTTRGN	EVISVMNRK	QAGKSVGVVT	TTRVQHASP	176
	*****.*	*:*:*:*:*:	.*:*:*:*:*:	** *:*:*:	.*:*:*:*:*:	*****.*	
Consensus	AYLCGVKXNX	TXGXSAAXX	XXXCNTTXGN	EVXSXXXXXAK	XXGKSVGXVT	TTRVXHAXPX	
TNALPrn	AAAYHSAARD	WYSDNEMPPE	ALSQGCKDIA	YQLMHNKIDI	DVIMGGGRKY	MYPKNRTDVE	235
TNALPmm	AAAYHSAARD	WYSDNEMPPE	ALSQGCKDIA	YQLMHNKIDI	DVIMGGGRKY	MYPKNRTDVE	235
TNALPhs	AAAYHSAARD	WYSDNEMPPE	ALSQGCKDIA	YQLMHNIRDI	DVIMGGGRKY	MYPKNKTDVE	235
TNALPcf	AAAYHSAARD	WYSDNEMPPE	ALSQGCKDIA	YQLMHNKIDI	EVIMGGGRKY	MFPKNRTDVE	213
TNALPfc	AAAYHSAARD	WYSDNEMPPE	ALSQGCKDIA	YQLMHNVRDI	EVIMGGGRKY	MFPKNRTDVE	235
TNALPbt	ASAYHSAARD	WYSDNEMPPE	ALSQGCKDIA	YQLMHNKIDI	EVIMGGGRKY	MFPKNRTDVE	235
GALPhs	GAYAHTVNRN	WYSDADVPAS	ARQEGCQDIA	TQLISNM-DI	DVILGGGRKY	MFPMTGPDPE	235
PLALPhs	GTIAHTVNRN	WYSDADVPAS	ARQEGCQDIA	TQLISNM-DI	DVILGGGRKY	MFRMTGPDPE	238
IALPhs	GTIAHTVNRN	WYSDADMPAS	ARQEGCQDIA	TQLISNM-DI	DVILGGGRKY	MFPMTGPDPE	235
	.*:*:*:*:	**** :*:~	* ..*:*:*:	**:*:*:	.*:*:*:*:	*: . . *	
Consensus	XXYAHXXXRX	WYSDXXXPPX	AXXXGCKDIA	XQLXXNXXDI	XVIXGGGRKY	MXXXXXXDXE	
TNALPrn	YELDEKARGT	RLDGLDLISI	WKSFKPRHKH	SHYVWNRTTEL	LALDPS-RVD	YLLGLFEPGD	294
TNALPmm	YELDEKARGT	RLDGLDLISI	WKSFKPRHKH	SHYVWNRTTEL	LALDPS-RVD	YLLGLFEPGD	294
TNALPhs	YESDEKARGT	RLDGLDLVDT	WKSFKPRYKH	SHFIWNRTTEL	LTLDPH-NVD	YLLGLFEPGD	294
TNALPcf	YEMDEKSTGA	RLDGLNLIDI	WKNFKPRHKH	SHYVWNRTTEL	LALDPY-TVD	YLLGLFDPGD	272
TNALPfc	YEMDEKARGT	RLDGLNLVDI	WKSFKPRHKH	SHYVWNRTTEL	LTLDPY-GVD	YLLGLFEPGD	294
TNALPbt	YELDEKARGT	RLDGLNLIDI	WKSFKPKHKH	SHYVWNRTDL	LALDPH-SVD	YLLGLFEPGD	294
GALPhs	YPDDYSQGGT	RLDGKNLVQE	WL---AKHQ	ARYVWNRTTEL	LQASLDPSVT	HLMLFEPGD	292
PLALPhs	YPDDYSQGGT	RLDGKNLVQE	WL---AKRQG	ARYVWNRTTEL	MQASLDPSVT	HLMLFEPGD	295
IALPhs	YPADASQNGI	RLDGKNLVQE	WL---AKHQ	AWYVWNRTTEL	MQASLDQSVT	HLMLFEPGD	292
	* * . *	**** :*~	* ..*:*:*:	: :~*:*:*:	: . *	:*:*:*:*:	
Consensus	YXXDXXXXGX	RLDGXXLXXX	WXXXXXXXXX	XXXXXWNRTXL	XXXXXXXVXX	XLXGLFXPGD	

FIG. 9 (cont'd)

TNALPrn	MQYELNRNLL	TDPSLSEMV	VALRILTKNP	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	354
TNALPmm	MQYELNRNLL	TDPSLSEMV	VALRILTKNL	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	354
TNALPhs	MQYELNRNNV	TDPSLSEMV	VAIQILRKNP	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	354
TNALPcf	MQYELNRNNV	TDPSLSEMV	IAIKILSKNP	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	332
TNALPfc	MQYELNRNST	TDPSLSEMV	IAIKILSKNP	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	354
TNALPbt	MQYELNRNNA	TDPSLSEMV	MAIRILNKNP	KGFFLLVEGG	RIDGHGHEGK	AKQALHEAVE	354
GALPhs	MKYEIHRDST	LDPSLMEVTE	AALLLSRNP	RGFFLFVEGG	RIDGHGHESR	AYRALTETIM	352
PLALPhs	MKYEIHRDST	LDPSLMEVTE	AALLLSRNP	RGFFLFVEGG	RIDGHGHESR	AYRALTETIM	355
IALPhs	TKYEIHRDPT	LDPSLMEVTE	AALLLSRNP	RGFFLFVEGG	RIDGHGHEGV	AYQALTEAVM	352
	:***::	**** **	*: * ::	:***:****	*****	* : ** *::	
Consensus	XXYEXRXXX	XDPSLXEMXX	XAXXXLXXXX	XGFXLXVEGG	RIDGHGHEXX	AXXALXEXXX	
TNALPrn	MDEAIGKAGT	MTSQKDTLTV	VTADHSHVFT	FGGYTPRGNS	IFGLAPMVSD	TDKKPFTAIL	414
TNALPmm	MDQAIGKAGA	MTSQKDTLTV	VTADHSHVFT	FGGYTPRGNS	IFGLAPMVSD	TDKKPFTAIL	414
TNALPhs	MDRAIGQAGS	LTSSDTLTV	VTADHSHVFT	FGGYTPRGNS	IFGLAPMLSD	TDKKPFTAIL	414
TNALPcf	MDRAIGKAGV	MTSLEDTLTV	VTADHSHVFT	FGGYTPRGNS	IFGLAPMVSD	TDKKPFTAIL	392
TNALPfc	MDQAIGRAGA	MTSVEDTLTI	VTADHSHVFT	FGGYTPRGNS	IFGLAPMVSD	TDKKPFTSIL	414
TNALPbt	MDQAIGQAGA	MTSVEDTLTV	VTADHSHVFT	FGGYTPRGNS	IFGLAPMVSD	TDKKPFTAIL	414
GALPhs	FDDAIERAGQ	LTSEEDTSL	VTADHSHVFS	FGGYPLRGSS	IFGLAPGKAR	-DRKAYTVLL	411
PLALPhs	FDDAIERAGQ	LTSEEDTSL	VTADHSHVFS	FGGYPLRGSS	IFGLAPGKAR	-DRKAYTVLL	414
IALPhs	FDDAIERAGQ	LTSEEDTLTL	VTADHSHVFS	FGGYTLRGSS	IFGLAPSKAQ	-DSKAYTSIL	411
	:* ** : **	:** :****:	*****:	****.***	*****	* * : * : *	
Consensus	XDXAIXXAGX	XTSXXDTLXX	VTADHSHVFX	FGGYXXRGXS	IFGLAPXXXX	XDXXXTXXL	
TNALPrn	YNGPGYKVV	DGERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFAK	GPMHLLHGV	474
TNALPmm	YNGPGYKVV	DGERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFAK	GPMHLLHGV	474
TNALPhs	YNGPGYKVV	GERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFSK	GPMHLLHGV	474
TNALPcf	YNGPGYKVV	GERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFAK	GPMHLLHGV	452
TNALPfc	YNGPGYKVV	GERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFAK	GPMHLLHGV	474
TNALPbt	YNGPGYKVV	GERENVSMV	DYAHNNYQAQ	SAVPLRHETH	GGEDVAVFAK	GPMHLLHGV	474
GALPhs	YNGPGYVLK	DGARDPVTE	ESGSPEYRQ	SAVPLDGETH	AGEDVAVFAR	GPQAHLVHGV	471
PLALPhs	YNGPGYVLK	DGARDPVTE	ESGSPEYRQ	SAVPLDEETH	AGEDVAVFAR	GPQAHLVHGV	474
IALPhs	YNGPGYVFN	SGVRPDVNES	ESGSPDYQQ	AAVPLSSETH	GGEDVAVFAR	GPQAHLVHGV	471
	*****	. * * : *	: . : * :	:****	***	*****	** * : * : *
Consensus	YNGPGYXXX	XGXRXXVXXX	XXXXXXVXXX	XAVPLXXETH	XGEDVAVFXX	GPXAHLVHGV	

FIG. 9 (cont'd)

TNALPrn	HEQNYIPHV	AYASCIG---	-ANLDHC	AWA	SSASSP	SPGA	LLLPLA	LFPL	RTLF-----	524
TNALPmm	HEQNYIPHV	AYASCIG---	-ANLDHC	AWA	SGSAP	SPGA	LLLPLA	VL	PTLF-----	524
TNALPhs	HEQNYVPHV	AYAACIG---	-ANLGH	CAPA	SSAGS	LAAGP	LLLALA	LYPL	SVLF-----	524
TNALPcf	HEQNYIPHV	AYAACIG---	-ANQDHC	CASA	SSAGG	SPSPG	LLLLLA	L	L	502
TNALPfc	HEQNYIPHV	AYAACIG---	-ANLDHC	CASA	SSAGG	SPSPG	LFLLLA	L	L	524
TNALPbt	QEQNYIPHV	AYAACIG---	-ANRDHC	CASA	SSSGS	SPSPG	LLLLLA	L	L	524
GALPhs	QEQTFIGHV	AFACLEPYT	ACDLAP	PRAGT	TDAAH	PGPSV	VPALLP	LLAG	TLLLTG	531
PLALPhs	QEQTFIGHV	AFACLEPYT	ACDLAP	PPAGT	TDAAH	PGRSV	VPALLP	LLAG	TLLLET	534
IALPhs	QEQSFIGHV	AFACLEPYT	ACDLAP	PPACT	TDAAH	P----	VAASLP	LLAG	TLLLGAS	527
Consensus	:**...***	*:*:*:	::	*	:	...	:	*::	*	:
	XEQXXXXHV	AXAXCXXXXX	XXXXXX	AXX	XXXXXX	XXXXX	XXXXL	XXXXX	XXLXXXXXX	
TNALPrn	-	(SEQ ID NO: 1210)								
TNALPmm	-	(SEQ ID NO: 1209)								
TNALPhs	-	(SEQ ID NO: 1208)								
TNALPcf	-	(SEQ ID NO: 1211)								
TNALPfc	-	(SEQ ID NO: 1207)								
TNALPbt	-	(SEQ ID NO: 1206)								
GALPhs	P 532	(SEQ ID NO: 1213)								
PLALPhs	P 535	(SEQ ID NO: 1214)								
IALPhs	P 528	(SEQ ID NO: 1212)								
Consensus	X	(SEQ ID NO: 1215)								

FIG. 10
ALP-TNALP Consensus Sequences Excluding Pathogenic Mutations

XXXXXXXXXX	XXXXXXXXXX	XXXXXXXXXX	PXXWXXXAXX	XLXXAXXLQX	XXXXXXXXAKNXI	60
XFLGDGMGVX	TVTAXRILKG	QXXXXXXXXGXEX	XLXMDXFFPX	ALSKTYXXXX	XVPDSXXTAT	120
AYLCGVKXNX	XTXGXSAAAX	XXXCNTTXGN	EVTSTXXXAK	XXGKSVGXVT	TTRVXHAXPX	180
XXYAHXXXXR	WYSDXXXXPX	AXXXGCXDIA	XQLXXNXXDI	XVIXGGGRKY	MXXXXXXXDXE	240
YXXDXXXXGX	RLDGXXLXXX	WXXXXXXXXXX	XXXXWNRTXL	XXXXXXXXXXVX	XLXGLFXPGD	300
MYEXXRXXX	XDPSLXEMXX	XAXXXLXXXX	XGFXLXVEGG	RIDHGHHEXX	AXXALXEXXX	360
XDXAIXXAGX	XTSXXDTLXX	VTADHSHVFX	FGGYXXRGXS	IFGLAPXXXX	XDXXKXTXXL	420
YGNPGYXXX	XGXRXXVXXX	XXXXXXXXYXXQ	XAVPLXXETH	XGEDVAVFXX	GPXAHLXHGV	480
XEQXXXXHVM	AXAXCXXXXX	XXXXXXXXAXX	XXXXXXXXXXXX	XXXXLXXXXX	XXLXXXXXXXX	540
					X	541

(SEQ ID NO: 1218)

FIG. 11
TNALP Consensus Sequences Excluding Pathogenic Mutations

MIXPFLXLAI	GTCXXXSXVP	EKEXDPXYWR	XQAQXTLKXA	LXLQXLNTNV	AKNXIMFLGD	60
GMGVSTVTAX	RILKGQLHHX	XGEETXLEMD	KFPXVALSKT	YNTNAQVPDS	AGTATAYLCG	120
VKANEGTVGV	SAATXRXXCNC	TTQGNEVTSI	LRWAKDXGKS	VGIVTTTRVN	HATPSAXYAH	180
SADRDWYSDN	EMPPEALSQG	CKDIAYQLMX	NXXDIXVIMG	GGRKYMXPKN	XTDVEYEXDE	240
KXXGXRLDGL	XLXXXWKXFK	PXXKHSXXXW	NRTXLLXLDP	XXVDYLLGLF	XPGDMQYELN	300
RNXXTDPSLS	EMVXXAXXIL	XKXXXGFFLL	VEGGRIDHGH	HEGKAKQALH	EAVEMDXAIG	360
XAGXXTSXXD	TLTXVTADHS	HVFTFGGYTP	RGNSIFGLAP	MXSDTDKKPF	TXILYGNPGP	420
YKVVXGEREN	VSMVDYAHNN	YQAQSAVPLR	HETHGGEDVA	VFXKGPM AHL	LHGVXEQNYX	480
PHVMAYAXCI	GANXXHCAXA	XSXXXXXXXXGX	LXLXAXXXX	XXLF		524

(SEQ ID NO: 1219)

FIG. 12
Multiple Sequence Alignment of Natriuretic Peptides

Human ANP	-----SLRRSS	CFGGRMDRIGAQSGGLGC	NSFRY-----	(SEQ ID NO: 1)
Human urodilatin	TAPRSLRRSS	CFGGRMDRIGAQSGGLGC	NSFRY-----	(SEQ ID NO: 2)
Human BNP	-SPKMVQSGG	CFGRKMDRISSSSGLGCKVLRH-----		(SEQ ID NO: 3)
Human CNP22	-----GLSKG	CFGLKLDRIGSMGSLGC	-----	(SEQ ID NO: 4)
DNP	-----EVKYDP	CFGHKIDRINHVSNLGCP	SLRDPNAPSTSA	(SEQ ID NO: 5)
	*** ::***. *.***			
CONSENSUS SEQUENCE		CFGXXXDRIXXXSXLGC		(SEQ ID NO: 6)

FIG. 13
Sequences of Human CNP53, CNP22, and CNP (ring only)

Human CNP53	DLRVDTKSRAAWARLLQEHFNARKYKGANKKGLSKG	CFGLKLDRI GSM SGLGC	(SEQ ID NO: 11)
Human CNP22	-----GLSKG	CFGLKLDRI GSM SGLGC	(SEQ ID NO: 4)
Human CNP (ring only)	-----	CFGLKLDRI GSM SGLGC	(SEQ ID NO: 12)

FIG. 14

Multiple Sequence Alignment of C-Type Natriuretic Peptides from Various Species

Human	-----GLSKG CFGLKLDRI GSM SLGC	(SEQ ID NO: 4)
Bovine	-----GLSKG CFGLKLDRI GSM SLGC	(SEQ ID NO: 13)
Sheep	-----GLSKG CFGLKLDRI GSM SLGC	(SEQ ID NO: 14)
Mouse	-----GLSKG CFGLKLDRI GSM SLGC	(SEQ ID NO: 15)
Pig	-----GLSKG CFGLKLDRI GSM SLGC	(SEQ ID NO: 16)
Micrurus fulvius fulvius	GLAKEALGDG CFGLKLDRI GTSS GLGC	(SEQ ID NO: 17)
Taeniopygia guttata	-----G CFGLKLDRI GTFF SLGC	(SEQ ID NO: 18)
Chicken	-----GLSR SCF GVKLDRI GSM SLGC	(SEQ ID NO: 19)
Rana catesbeiana	-----SRG CF GVKLDRI GA FS GLGC	(SEQ ID NO: 20)
Eel	-----GWN RG CFGLKLDRI GS LS GLGC	(SEQ ID NO: 21)
Trout	-----GWN RG CFGLKLDRI GSM SLGC	(SEQ ID NO: 22)
Ornithorhynchus anatinus	-----GLSKG CFGLKLDRI GST SLGC	(SEQ ID NO: 23)
Trimeresurus flavoviridis	-----KG CF GHKLDRI GS TS GLGC	(SEQ ID NO: 24)
Polypterus endlicheri	-----SKG CF GLKLDRI GS IS GLGC	(SEQ ID NO: 25)
Xenopus laevis	-----LSKG CF GLKLDRI GV SV SLGC	(SEQ ID NO: 26)
Oryzias latipes	-----G CF GMKMDRI GS IS GLGC	(SEQ ID NO: 27)
Tetraodon nigroviridis	-----G CF GMKIDRI GS IS GLGC	(SEQ ID NO: 28)
Pseudechis australis	-----SKIGD GCF GLPLDHI GS VS GLGC	(SEQ ID NO: 29)
CONSENSUS SEQUENCE	XXXXXXX XXXXXCF GX XXDXIGXX SLGC *** :*:*** *****	(SEQ ID NO: 30)

FIG. 15A**Multiple Alignment of C-Type Natriuretic Peptides from Various Species**

```

sp|Q8AYR5|ANFC2_ORYLA      ---MAVCSSSS-----LILLTVFLSVAVETRP--SSDRDE----- 30
sp|Q805D5|ANFC2_TAKRU      ---MAASSSSF-----VPLVLLFLAIPVEPRP--SMTRDE----- 30
sp|Q76KW6|ANFC_ACITR       ---MSISSSSSSSSSSSSCLLLISLMLLAASCQGRPDLQHRNH----- 40
sp|Q61839|ANFC_MOUSE       ---MHLSQLI-----ACALLLALLSLRPSEAKPGTP----- 28
tr|Q544K5|Q544K5_MOUSE     ---MHLSQLI-----ACALLLALLSLRPSEAKPGTP----- 28
tr|Q8VHG9|Q8VHG9_NOTAL     ---MHLSQLI-----ACALLLALLSLRPSEAKPGTP----- 28
sp|P55207|ANFC_RAT         ---MHLSQLI-----ACALLLALLSLRPSEAKPGTP----- 28
sp|P55206|ANFC_BOVIN       ---MHLSQLL-----ACALLLALLSLRPSEAKPGAP----- 28
sp|P56283|ANFC_SHEEP       ---MHLSQLL-----ACALLSLLSLRPSEAKPGAP----- 28
sp|P18104|ANFC_PIG         ---MHLSQLL-----ACALLLTLLSLRPSEAKPGAP----- 28
sp|P23582|ANFC_HUMAN       ---MHLSQLL-----ACALLLTLLSLRPSEAKPGAP----- 28
sp|P84715|ANF39_ORNAN      ---MHLSHLL-----AWALLLTLLSLR--AEAKPPSPQ----- 28
tr|Q9QZ96|Q9QZ96_CAVPO     -----
sp|Q80017|ANFC4_ORYLA      ---MNL SYLV-----ACGLLVTFLSDK--MDAQPLTPAQ----- 29
sp|Q805D3|ANFC4_TAKRU      ---MNL SYLV-----ACGLMITLLSVR--MGAKPLSQAQ----- 29
tr|C1BXI5|C1BXI5_ESOLU     ---MNL SYLV-----ACGLMITLLSVR--SGAKPLTAAQ----- 29
tr|D2KXA5|D2KXA5_ANGJA     ---MNVSQLM-----VCGLLMALFSFS--TEAKSLIPAQ----- 29
tr|Q1XGY7|Q1XGY7_9ACTI     ---MNL SHLV-----ACGLLVALLTVT--MEAKPLTQSQ----- 29
sp|P40756|ANFD_RANCA       ---MHFCHIV-----CWGLVLAVLYLR--TEAKPVAQAH----- 29
sp|P0C7P5|BNP_TRIFL        ---MFVSRLA-----ASGLLLLALLLALSLDGKPVHQS KPGR----- 33
sp|P0C7P6|BNP_TRIGA        ---MFVSRLA-----ASGLLLLALLLALSLDGKPVQE--KPGR----- 32
sp|Q6LEM5|BNP1_BOTJA       ---MVL SRLA-----ASGLLLLALLLALSVDGKPVQQWAQS----- 32
sp|Q9PW56|BNP2_BOTJA       ---MVL SRLA-----ASGLLLLALLLALSVDGKPVQQWAQGG----- 33
sp|P68515|BNP_BOTIN        ---MVL SRLA-----ASGLLLLALLLALSVDGKPVQQWAQGG----- 33
sp|Q90Y12|BNP_CRODU        ---MFVSRLA-----ASGLLLLALLLAVSLDGKPLQQWS----- 30
sp|Q2PE51|BNP_CRODO        ---MFVSRLA-----ASGLLLLALLLAVSLDGKPLQQWS----- 30
sp|B0VXV8|BNP_SISCA        ---MFVSRLA-----ASGLLLLALLLAVSLDGKPVQQWS----- 30
sp|Q27J49|BNP_LACMU        ---MFVSRLA-----ASGLLLLALLLAVSLDGKPVQQWSH----- 31
sp|P01021|BNP_AKGHA        ---MFVSRLA-----ASGLLLLALMALSLDGKPVQQWSQGRPPGPPI 39
sp|Q09GK2|VNP_PHIOL        ---MVASRLA-----AGGLLLLALLLALALDGKPAPP--QP----- 30
tr|D1MZV3|D1MZV3_RHATT     ---MFASRLA-----ALG LLLLALV---LDGKPAPPPQP----- 28
tr|Q7T1M4|Q7T1M4_BOTJR     ---HEKPSRSG-----AKSAAVGA KLAASSD SAADECSSGRK----- 34
tr|Q402A2|Q402A2_PETMA     -----
tr|Q402A3|Q402A3_LAMJA     ---MKLQLLMMV-----VVVGSWTF LG---VGAKPLT SYELYD----- 32
tr|Q402A1|Q402A1_9PETR     ---MRRQVLVMV-----VMVVVMVMSGKSVTAKPVASYELLD----- 35
sp|P21805|ANFC_CHICK       -----
tr|A9CDT6|A9CDT6_CHICK     ---MKLLFC-----PGFFLLLIVSQKQAMAKPIS----- 26
sp|P20968|ANFC_RANCA       ---MSYKRGTC-----LGFIMLLMVSHHHTKGKPLS----- 28
sp|P55208|ANFC_TRISC       ---MSGQTSFY-----CGLLLVLLIQAQ---ARPRS----- 25
sp|P23259|ANFC_SCYCA       -----RPRS----- 4
sp|P41319|ANFC_SQUAC       ---MSGHTSFY-----CGLLLLLLIQVQ---ARPR----- 25
tr|Q2MH72|Q2MH72_9CHON     ---MSGNTNFY-----CGLVLLLLLLQVQ---GRPRS----- 25
tr|Q2MH73|Q2MH73_9CHON     ---MSGNTNFY-----CGLVLLLLLLQVQ---GRPRS----- 25
tr|Q2MH71|Q2MH71_9CHON     ---MSGNTNFY-----CGLVLLLLLLQVQ---GRPRS----- 25
tr|Q2MH74|Q2MH74_DASAK     ---MSGNTNFY-----CGLVLLLLLLQVQ---GRPRS----- 25
tr|Q2PF87|Q2PF87_CALMI     ---MNAHVSFP-----CGLMLLLLIIQVQVQ---ARPTG----- 28
sp|Q80018|ANFC3_ORYLA      ---MSLRAF-----MLCVCLLLQSVG---ARPAS----- 23
tr|Q4ADV1|Q4ADV1_ORYLA     ---MSLRAF-----MLCVCLLLQSVG---ARPAS----- 23
sp|Q805D4|ANFC3_TAKRU      ---MSLNLPGY-----ALFFILLVASSG---AKPAP----- 25
tr|C0H7B0|C0H7B0_SALSA     ---MKMISNIQFF-----CLTALVLLNLVG---ANPMS----- 27
tr|C1BWD1|C1BWD1_ESOLU     ---MISNIQFC-----CLSVLVLLNLVG---AKPVS----- 25
tr|D2KXA3|D2KXA3_ANGJA     ---MISNITIY-----CISLLFLNLVG---GKPVS----- 25
tr|B3DJJ2|B3DJJ2_DANRE     ---MIANISVF-----CVSSLLLLNLVG---AKPVS----- 25
tr|Q1XGY8|Q1XGY8_9ACTI     ---MVSRLTVY-----CALFIIVLSQVS---AKPVS----- 25
sp|Q8AXR2|ANFC2_ONCMY      ---ML--YPA-----LLCAALLLIAPLGHTEGRTL YPSPD----- 30
sp|Q8AXR3|ANFC1_ONCMY      ---ML--YPA-----LLCAALLLIAPLGHTEGRTL HPSPD----- 30
tr|C1BKS8|C1BKS8_OSMO      ---ML--CPV-----LLCATLVLLPPELSEGRALHPSPE----- 30
tr|Q805E7|Q805E7_OREMO     ---ML--CPV-----LLCAALLLLTPLEITEARALHPSPD----- 30
tr|C3KH23|C3KH23_ANOFI     ---ML--CPV-----LLCATLLLLTPLEITEARALHPPPD----- 30
sp|Q8AYR6|ANFC1_ORYLA      ---ML--CPV-----LLCATLLLLTPFEVTEARALHPSAD----- 30
sp|Q805D6|ANFC1_TAKRU     ---ML--CPA-----LLCAALLLLTPVEITDARALQQPSD----- 30
sp|P18145|ANFC_ANGJA       ---MM--CKA-----LVFAVLLLAVPLERADSRALRTPVD----- 30
tr|Q1XGY9|Q1XGY9_9ACTI     ---MMGSCSAPLLTGHRILCLFLLMASSLSPIHSRAFRSPP----- 38
tr|A9CDT5|A9CDT5_CHICK     MLGLPA-----WPCSLFLLLVLLSASVQAMSSSGQR----- 31

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FIG. 15B**Multiple Alignment of C-Type Natriuretic Peptides from Various Species**

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sp|Q8AYR5|ANFC2_ORYLA -----
sp|Q805D5|ANFC2_TAKRU -----
sp|Q76KW6|ANFC_ACITR -----
sp|Q61839|ANFC_MOUSE -----
tr|Q544K5|Q544K5_MOUSE -----
tr|Q8VHG9|Q8VHG9_NOTAL -----
sp|P55207|ANFC_RAT -----
sp|P55206|ANFC_BOVIN -----
sp|P56283|ANFC_SHEEP -----
sp|P18104|ANFC_PIG -----
sp|P23582|ANFC_HUMAN -----
sp|P84715|ANF39_ORNAN -----
tr|Q9QZ96|Q9QZ96_CAVPO -----
sp|Q80017|ANFC4_ORYLA -----
sp|Q805D3|ANFC4_TAKRU -----
tr|C1BXI5|C1BXI5_ESOLU -----
tr|D2KXA5|D2KXA5_ANGJA -----
tr|Q1XGY7|Q1XGY7_9ACTI -----
sp|P40756|ANFD_RANCA -----
sp|P0C7P5|BNP_TRIFL -----SPPIS----- 38
sp|P0C7P6|BNP_TRIGA -----SPPISPLLVP-----PPPPPHWPPP- 53
sp|Q6LEM5|BNP1_BOTJA -----WP--GNIPPLKVQQWAQGGWPRPGPEIPPLTVQQWAQN- 69
sp|Q9PW56|BNP2_BOTJA -----WPRPGPEIPPLKVQQWAQGGWPRPGPEIPPLTVQQWAQN- 72
sp|P68515|BNP_BOTIN -----WPRPGPEIPPLKVQQWAQGGWPRPGPEIPPLTVQQWAQN- 72
sp|Q90Y12|BNP_CRODU -----QRWP--- 34
sp|Q2PE51|BNP_CRODO -----QRWP--- 34
sp|B0VXV8|BNP_SISCA -----QNWPG-- 35
sp|Q27J49|BNP_LACMU -----KGWPPERQIPPLVVQWSQKPWP-PGHHIPPVVQEWPP-- 69
sp|P01021|BNP_AGKHA PRLVVQWSQGLPPGPPIPRLVVQWSQG-LP-PGPPIPPLVVQWSQGL 87
sp|Q09GK2|VNP_PHIOL -----
tr|D1MZV3|D1MZV3_RHATT -----
tr|Q7T1M4|Q7T1M4_BOTJR -----GEPPG- 39
tr|Q402A2|Q402A2_PETMA -----
tr|Q402A3|Q402A3_LAMJA -----
tr|Q402A1|Q402A1_9PETR -----
sp|P21805|ANFC_CHICK -----
tr|A9CDT6|A9CDT6_CHICK -----
sp|P20968|ANFC_RANCA -----
sp|P55208|ANFC_TRISC -----
sp|P23259|ANFC_SCYCA -----
sp|P41319|ANFC_SQUAC -----
tr|Q2MH72|Q2MH72_9CHON -----
tr|Q2MH73|Q2MH73_9CHON -----
tr|Q2MH71|Q2MH71_9CHON -----
tr|Q2MH74|Q2MH74_DASAK -----
tr|Q2PF87|Q2PF87_CALMI -----
sp|Q80018|ANFC3_ORYLA -----
tr|Q4ADV1|Q4ADV1_ORYLA -----
sp|Q805D4|ANFC3_TAKRU -----
tr|C0H7B0|C0H7B0_SALSA -----
tr|C1BWD1|C1BWD1_ESOLU -----
tr|D2KXA3|D2KXA3_ANGJA -----
tr|B3DJJ2|B3DJJ2_DANRE -----
tr|Q1XGY8|Q1XGY8_9ACTI -----
sp|Q8AXR2|ANFC2_ONCMY -----
sp|Q8AXR3|ANFC1_ONCMY -----
tr|C1BKS8|C1BKS8_OSMMO -----
tr|Q805E7|Q805E7_OREMO -----
tr|C3KH23|C3KH23_ANOFI -----
sp|Q8AYR6|ANFC1_ORYLA -----
sp|Q805D6|ANFC1_TAKRU -----
sp|P18145|ANFC_ANGJA -----
tr|Q1XGY9|Q1XGY9_9ACTI -----
tr|A9CDT5|A9CDT5_CHICK -----

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FIG. 15C**Multiple Alignment of C-Type Natriuretic Peptides from Various Species**

```

sp|Q8AYR5|ANFC2_ORYLA      -----
sp|Q805D5|ANFC2_TAKRU      -----
sp|Q76KW6|ANFC_ACITR       -----
sp|Q61839|ANFC_MOUSE       -----
tr|Q544K5|Q544K5_MOUSE     -----
tr|Q8VHG9|Q8VHG9_NOTAL     -----
sp|P55207|ANFC_RAT         -----
sp|P55206|ANFC_BOVIN       -----
sp|P56283|ANFC_SHEEP       -----
sp|P18104|ANFC_PIG         -----
sp|P23582|ANFC_HUMAN       -----
sp|P84715|ANF39_ORNAN      -----
tr|Q9QZ96|Q9QZ96_CAVPO     -----
sp|Q80017|ANFC4_ORYLA      -----
sp|Q805D3|ANFC4_TAKRU      -----
tr|C1BXI5|C1BXI5_ESOLU     -----
tr|D2KXA5|D2KXA5_ANGJA     -----
tr|Q1XGY7|Q1XGY7_9ACTI     -----
sp|P40756|ANFD_RANCA       -----
sp|P0C7P5|BNP_TRIFL       -----PLSAQQWMPEGRPPHP--IPPLSVQQWSQGRP----- 68
sp|P0C7P6|BNP_TRIGA       ---HHIPPLSVQKFPFGWKPTHPHHIPPLEVQQWSQGGP----- 89
sp|Q6LEM5|BNP1_BOTJA       WPHPQIPPLTVQQWAQ-GRAPGPP-IPPLTVQQWAQGRAPHPPIPPAPLQ 117
sp|Q9PW56|BNP2_BOTJA       WPHPQIPPLTVQQWAQWGRPPGPP-IPPLTVQQWAQARPPHPPIPPAPLQ 121
sp|P68515|BNP_BOTIN        WPHPQIPPLTVQQWAQLGPPPRPQ-IPPLEVQQWAQGRAPHPPIPPAPLQ 121
sp|Q90Y12|BNP_CRODU        -----HLE-IPPLVVQNWK----- 47
sp|Q2PE51|BNP_CRODO        -----HLE-IPPLVVQNWK----- 47
sp|B0VXV8|BNP_SISCA        ---PKVPPLVVQQWSQN--WPHPQ-IPPLVVQNWK----- 64
sp|Q27J49|BNP_LACMU        --GHHIPPLVVQQWSQKKWPPGHH-IPPLVVQKWDP----- 102
sp|P01021|BNP_AGKHA        PPRPKIPPLVVQQWSQG-LPPRPK-IPPLVVQKWDP----- 121
sp|Q09GK2|VNP_PHIOL       -----
tr|D1MZV3|D1MZV3_RHATT     -----
tr|Q7T1M4|Q7T1M4_BOTJR     ---PIIPPLTVQQWAQAR-PPHPP-IPPAPLQKWAPVQK----- 73
tr|Q402A2|Q402A2_PETMA     -----
tr|Q402A3|Q402A3_LAMJA     -----
tr|Q402A1|Q402A1_9PETR     -----
sp|P21805|ANFC_CHICK       -----
tr|A9CDT6|A9CDT6_CHICK     -----
sp|P20968|ANFC_RANCA       -----
sp|P55208|ANFC_TRISC       -----
sp|P23259|ANFC_SCYCA       -----
sp|P41319|ANFC_SQUAC       -----
tr|Q2MH72|Q2MH72_9CHON     -----
tr|Q2MH73|Q2MH73_9CHON     -----
tr|Q2MH71|Q2MH71_9CHON     -----
tr|Q2MH74|Q2MH74_DASAK     -----
tr|Q2PF87|Q2PF87_CALMI     -----
sp|Q80018|ANFC3_ORYLA      -----
tr|Q4ADV1|Q4ADV1_ORYLA     -----
sp|Q805D4|ANFC3_TAKRU      -----
tr|C0H7B0|C0H7B0_SALSA     -----
tr|C1BWD1|C1BWD1_ESOLU     -----
tr|D2KXA3|D2KXA3_ANGJA     -----
tr|B3DJJ2|B3DJJ2_DANRE     -----
tr|Q1XGY8|Q1XGY8_9ACTI     -----
sp|Q8AXR2|ANFC2_ONCMY      -----
sp|Q8AXR3|ANFC1_ONCMY      -----
tr|C1BKS8|C1BKS8_OSMMO     -----
tr|Q805E7|Q805E7_OREMO     -----
tr|C3KH23|C3KH23_ANOFI     -----
sp|Q8AYR6|ANFC1_ORYLA      -----
sp|Q805D6|ANFC1_TAKRU      -----
sp|P18145|ANFC_ANGJA       -----
tr|Q1XGY9|Q1XGY9_9ACTI     -----
tr|A9CDT5|A9CDT5_CHICK     -----

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FIG. 15D

Multiple Alignment of C-Type Natriuretic Peptides from Various Species

sp Q8AYR5 ANFC2_ORYLA	-----EQVLKSLFGPHLTSL-----IL	47
sp Q805D5 ANFC2_TAKRU	-----AQVLRALFGARLSSI-----IS	47
sp Q76KW6 ANFC_ACITR	-----KSQLAGLFGAEVAAL-----LE	57
sp Q61839 ANFC_MOUSE	-----PKVPRTPPGEEELADS-----QAAG	47
tr Q544K5 Q544K5_MOUSE	-----PKVPRTPPGEEELADS-----QAAG	47
tr Q8VHG9 Q8VHG9_NOTAL	-----PKVPRTPPGEEELADS-----QAAG	47
sp P55207 ANFC_RAT	-----PKVPRTPPGEEELAEP-----QAAG	47
sp P55206 ANFC_BOVIN	-----PKVPRTPPGEEELAEP-----QAAG	47
sp P56283 ANFC_SHEEP	-----PKVPRTPPGEEELAEP-----QAAG	47
sp P18104 ANFC_PIG	-----PKVPRTPPGEEELAEP-----QAAG	47
sp P23582 ANFC_HUMAN	-----PKVPRTPPAEEELAEP-----QAAG	47
sp P84715 ANF39_ORNAN	-----PQVPRSP-GDEASEA-----VAAN	46
tr Q9QZ96 Q9QZ96_CAVPO	-----	
sp Q80017 ANFC4_ORYLA	-----QKSLRSLLGEEELAEF-----LESG	48
sp Q805D3 ANFC4_TAKRU	-----QKSFRSLLGEEELAEF-----LESE	48
tr C1BXI5 C1BXI5_ESOLU	-----QKSLRNLLGEEELSEF-----LASG	48
tr D2KXA5 D2KXA5_ANGJA	-----EKSLRNLLGEEELSEY-----LASG	48
tr Q1XGY7 Q1XGY7_ACTI	-----QKSLRNLLGEEELSAI-----LTSD	48
sp P40756 ANFD_RANCA	-----QKSLRALLGEEELAEY-----LVSG	48
sp P0C7P5 BNP_TRIFL	---RSEVPPVVVQPHESPAGGTTAFREELSPG-----PEAASG	103
sp P0C7P6 BNP_TRIGA	---RSEL---VQPHESPAGGTTAFREELSLG-----PEAASG	120
sp Q6LEM5 BNP1_BOTJA	KWAPLQKWAPLLQPHESPASGTTALREELSLG-----PEAASG	155
sp Q9PW56 BNP2_BOTJA	KWAPVQKWAPLLQPHESPASGTTALREELSLG-----PEAASG	159
sp P68515 BNP_BOTIN	KWAPVQKWAPLLQPHESPASGTTALREELSLG-----PEAASG	159
sp Q90Y12 BNP_CRODU	-----SPTQLQARESPAGGTTALREELSLG-----PEAALD	78
sp Q2PE51 BNP_CRODO	-----SPTQLQARESPAGGTTALREELSLG-----PEAALD	78
sp B0VXV8 BNP_SISCA	-----SPTQLQPRESPAGGTTALREELSLG-----PDAALD	95
sp Q27J49 BNP_LACMU	---PPI-SPPLLKPHESPAGGTTALREELSLG-----PEAALD	136
sp P01021 BNP_AGKHA	---PPVSPPLLKPHESPAGGTTALREELSLG-----PEAASG	156
sp Q09GK2 VNP_PHIOL	-----LRKAPAGGTTAWRRELTEQ-----PEGASR	55
tr D1MZV3 D1MZV3_RHATT	-----LRKAPAGGTTALQRQLTEQQQQQQ-----QAEQSSG	59
tr Q7T1M4 Q7T1M4_BOTJR	-WAPVQKWAPLLQPHESPAGGTTALREELSLG-----PEAASG	110
tr Q402A2 Q402A2_PETMA	-----SGSEPWEGG-FLPRVSSSSSSSSG-----EVEPLAE	30
tr Q402A3 Q402A3_LAMJA	-----DAGSEPWEGG-FLPRISSSSSSSS-----AERLAD	60
tr Q402A1 Q402A1_9PETR	-----DTNSEPWEGGSLPSLPSQGEED-----SHPLS-	63
sp P21805 ANFC_CHICK	-----	
tr A9CDT6 A9CDT6_CHICK	-----SLQSLSMILLDEE-----L	39
sp P20968 ANFC_RANCA	-----SLQNLRLLEDN-----F	41
sp P55208 ANFC_TRISC	-----DDSLQTLRLLEDE-----Y	40
sp P23259 ANFC_SCYCA	-----DDSLQTLRLLEDE-----Y	19
sp P41319 ANFC_SQUAC	-----DDSLQVLSRLLEDE-----Y	40
tr Q2MH72 Q2MH72_9CHON	-----DDSLQALTRLLEDE-----Y	40
tr Q2MH73 Q2MH73_9CHON	-----DDSLQALTRLLEDE-----Y	40
tr Q2MH71 Q2MH71_9CHON	-----DDSLQALTRLLEDE-----Y	40
tr Q2MH74 Q2MH74_DASAK	-----DDSLQALTRLLEDE-----Y	40
tr Q2PF87 Q2PF87_CALMI	-----VDSLQILSRLEDE-----Y	43
sp Q80018 ANFC3_ORYLA	-----ELQNLERLL-----	32
tr Q4ADV1 Q4ADV1_ORYLA	-----ELQNLERLL-----	32
sp Q805D4 ANFC3_TAKRU	-----DLQILEPPLSSLEEQQEEMQEEVQEKVQEQQEEVQ	59
tr C0H7B0 C0H7B0_SALSA	-----NLQSLKQLLEEE-----SH	41
tr C1BWD1 C1BWD1_ESOLU	-----NLQSLKEFLEE-----SN	38
tr D2KXA3 D2KXA3_ANGJA	-----SLQSLKELLEEE-----SN	39
tr B3DJJ2 B3DJJ2_DANRE	-----SLQSLKQLLEDE-----VN	39
tr Q1XGY8 Q1XGY8_ACTI	-----SLQSFAQLLEDE-----SN	39
sp Q8AXR2 ANFC2_ONCMY	-----AIQFVEQFLDR-----YN	43
sp Q8AXR3 ANFC1_ONCMY	-----AIQFVEQFLDR-----YN	43
tr C1BKS8 C1BKS8_OSMMO	-----GLQFVEQFLER-----CT	43
tr Q805E7 Q805E7_OREMO	-----AVQFVEQFLER-----YN	43
tr C3KH23 C3KH23_ANOFI	-----AVQFMEQFLER-----YN	43
sp Q8AYR6 ANFC1_ORYLA	-----AVQFVEQFLDR-----YN	43
sp Q805D6 ANFC1_TAKRU	-----AAQFMEQFLER-----YN	43
sp P18145 ANFC_ANGJA	-----AIQFVEQFLEH-----YN	43
tr Q1XGY9 Q1XGY9_ACTI	-----LQFLSTLLEKE-----YG	51
tr A9CDT5 A9CDT5_CHICK	-----LQVLLSLLPS-----DS	44

FIG. 15E

Multiple Alignment of C-Type Natriuretic Peptides from Various Species

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sp|Q8AYR5|ANFC2_ORYLA      APPTSND--TEGSSGSPEPP-----TPSEAPVLIH-- 76
sp|Q805D5|ANFC2_TAKRU      TPVNTDDI--AELLRRPGPPR-----SFGASPGALRGLTR-- 81
sp|Q76KW6|ANFC_ACITR       DAGAADGSSGEEAALSQRAPPS-----IRALHPRSGRLGLRDD 95
sp|Q61839|ANFC_MOUSE       GNQKKGDKTPGSGGANLKGDRS-----RLLRDRLR 76
tr|Q544K5|Q544K5_MOUSE     GNQKKGDKTPGSGGANLKGDRS-----RLLRDRLR 76
tr|Q8VHG9|Q8VHG9_NOTAL     GNQKKGDKTPGGGGANLKGDRSRLKGDTPGGGGANLKGDRSRLLRDLR 97
sp|P55207|ANFC_RAT         GNQKKGDKTPGGGGANLKGDRS-----RLLRDRLR 76
sp|P55206|ANFC_BOVIN       GGQKKGDKTPGGGGANLKDDRS-----RLLRDRLR 76
sp|P56283|ANFC_SHEEP       GGQKKGDKTPGGGGANLKDDRS-----RLLRDRLR 76
sp|P18104|ANFC_PIG         GGQKKGDKTPGGGGANLKGDRS-----RLLRDRLR 76
sp|P23582|ANFC_HUMAN       GGQKKGDKAPGGGGANLKGDRS-----RLLRDRLR 76
sp|P84715|ANF39_ORNAN      GGKKKGDKP-----KGRDP-----RLLRELR 68
tr|Q9QZ96|Q9QZ96_CAVPO    -----
sp|Q80017|ANFC4_ORYLA      ENENRLDDVRSRM-----RLLRDRLR 68
sp|Q805D3|ANFC4_TAKRU      EKERRLDAVRSRL-----RLLRDRLR 68
tr|C1BXI5|C1BXI5_ESOLU     ERERRLDTVRSRV-----RLLRDRLR 68
tr|D2KXA5|D2KXA5_ANGJA     ERERNLESARS-----RLLRDRLR 66
tr|Q1XGY7|Q1XGY7_9ACTI     EQESGSENLRSA-----RLLRDRLR 68
sp|P40756|ANFD_RANCA       ERGERSIDPKTRA-----RLLRDIR 68
sp|P0C7P5|BNP_TRIFL       -----PAAPHRLPKSKG-----ASATS-AASRPMRDRLR 130
sp|P0C7P6|BNP_TRIGA       -----PAAPQRLPKRKG-----ASATS-AASRSMRDRLR 147
sp|Q6LEM5|BNP1_BOTJA       VPSAGAEVGRSGSK-APAAPHRLSKSKG-----AAAT-----RPMRDRLR 193
sp|Q9PW56|BNP2_BOTJA       VPSAGAEVGRSGSK-APAAPHRLSKSKG-----AAATS-AASRPMRDRLR 201
sp|P68515|BNP_BOTIN        VPSAGAEVGRSGSK-APAAPHRLSKSKG-----AAATS-AASRPMRDRLR 201
sp|Q90Y12|BNP_CRODU        TPPAGPDGGRSGSKAAAAAPQRLSKSKG-----ASATS-AASR---DLR 118
sp|Q2PE51|BNP_CRODO        TPPAGPDGGRSGSKAAAAAPQRLSKSKG-----ASATS-AASR---DLR 118
sp|B0VXV8|BNP_SISCA        TPPAGPDVGRSGSK-AAAAPQRLSKSKG-----ASATS-TASRPMRDRLR 137
sp|Q27J49|BNP_LACMU        TPPAGPDVGRSGSK-APAAPHRLPKSKG-----ASATS-AASRPMRDRLR 178
sp|P01021|BNP_AGKHA        PAAAGADGGRSGSK-APAALHRLSKSKG-----ASATSASASRPMRDRLR 199
sp|Q09GK2|VNP_PHIOL        PAAGGGGGGRSGSKAANAAPTAPKSKG-----AAAAAAAARLMRDRLR 100
tr|D1MZV3|D1MZV3_RHATT     PAAGGGGG--RSGSKTANAAPTAPKSKG-----AAASAASRLLRDLR 99
tr|Q7T1M4|Q7T1M4_BOTJR     VPSAGAEGRAQRLEGARCTPSAVEEQRGG-----GDLGGVAADAGLAPRR 155
tr|Q402A2|Q402A2_PETMA     VTATGGVSGGVSGVLGGTPWVGPRGHQ-----RPSRGLA 65
tr|Q402A3|Q402A3_LAMJA     ATVTR-HGGGGGGGGDDGTSWELPQGPPG-----PPRSSRGLA 97
tr|Q402A1|Q402A1_9PETR     -----AEGG-----PWERGSGPQ-----RSSRGIG 83
sp|P21805|ANFC_CHICK       -----
tr|A9CDT6|A9CDT6_CHICK     QHPLVSEERDREQDGSIPVGAF-----DQEDAEPQWTRNTRD----- 76
sp|P20968|ANFC_RANCA       ERSFGSDEADQQL---VPTDSL-----DQLDPELQWNKNRLE----- 75
sp|P55208|ANFC_TRISC       GHYLPSEDLNNEAQEMSPAASLPEFNADQSDLELPWDRESRE----- 82
sp|P23259|ANFC_SCYCA       GHYLPSEDLNNEAEEMSPAASLPELNADQSDLELPWRESRE----- 61
sp|P41319|ANFC_SQUAC       GHFN-SEELNNEAQEISPAASLPDLNTDQSDLELPWDRESRE----- 81
tr|Q2MH72|Q2MH72_9CHON     GQYFTTEDLNNEAPEIPPAASLPDLNTDQSDLDLSWDRESRE----- 82
tr|Q2MH73|Q2MH73_9CHON     GQYFTTEDLNNEAPEIPPAASLPDLNTDQSDLDLSWDRESRE----- 82
tr|Q2MH71|Q2MH71_9CHON     GQYFTSEDLNNEAPEIPPAASLPDLNTDQPDFDLSDWDRESRE----- 82
tr|Q2MH74|Q2MH74_DASAK     GQYFTSEDLNNEAPEMSPAASLPDLNTEQSETDLPWDRESRE----- 82
tr|Q2PF87|Q2PF87_CALMI     GPYLSSEDSMEAEASRAGTLRLDNLQADMDLLWDRDARD----- 85
sp|Q80018|ANFC3_ORYLA      ---QDQLSSTEHPPEE---DRLD---RTREEPQLGG----- 58
tr|Q4ADV1|Q4ADV1_ORYLA     ---QDQLSSTEHPPEE---DRLD---RTREEPQLGG----- 58
sp|Q805D4|ANFC3_TAKRU      EKVQEQQEEVQEQQEEVQEQE-----EQQEEVQERGRGTGDVLLRAQLD 104
tr|C0H7B0|C0H7B0_SALSA     VPHYASDEMVGDKDLNTEN-----IAEEVPPWDSER----- 75
tr|C1BWD1|C1BWD1_ESOLU     VPYYGSESEVDKDLNTEKEA-----FTGEVVPWLTEDR----- 74
tr|D2KXA3|D2KXA3_ANGJA     APYLDSEEAQVQKEMNAENAA-----FTKASLHSDWPNSR----- 75
tr|B3DJJ2|B3DJJ2_DANRE     KPFEESQESVMEQKDATAEKSA-----LDERAEQLWESDAR----- 75
tr|Q1XGY8|Q1XGY8_9ACTI     HPYVSDDDTRGGLDVSAEIAT-----DDSEADIPWNHNRDL----- 77
sp|Q8AXR2|ANFC2_ONCMY      DLT--LDDLLENLVSSQPEEPSS-----AFTSGVKIAEYPKW 77
sp|Q8AXR3|ANFC1_ONCMY      DLT--LDDLLENLVSSQPEEPSS-----AFTSGVKVAEYPKW 77
tr|C1BKS8|C1BKS8_OSMO      DLLN-LDDLLENAGSNQPEEPS-----DYANGVKVAEYPKW 77
tr|Q805E7|Q805E7_OREMO     DLLT-LDDLLENMLNSQAEQES-----TLSSGSKAVEYPKW 77
tr|C3KH23|C3KH23_ANOFI     DLLT-LDDLLENLINSQPEEQS-----TFSSGVKAAEYPKW 77
sp|Q8AYR6|ANFC1_ORYLA      DLLT-LDDLLENLNTQPEEQS-----TLSSGVKTAIEYPKW 77
sp|Q805D6|ANFC1_TAKRU     DLLT-LDDLLENMLNSHPEDQS-----NLSS-SKADEYPKW 76
sp|P18145|ANFC_ANGJA       DLLN-IDDLLENQTDQLESPO-----PLSSGLKVAEYPKW 77
tr|Q1XGY9|Q1XGY9_9ACTI     NLQSGPVNIHNVSSSEQYEDPQ-----PWADVSSVSKEQIWI 86
tr|A9CDT5|A9CDT5_CHICK     ESMPAEEDMKEGSSSEPQLLSP-----PLPLLPSSRAR----- 76

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FIG. 15F

Multiple Alignment of C-Type Natriuretic Peptides from Various Species

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sp|Q8AYR5|ANFC2_ORYLA      -----GDRGTASQILRSFLRQRE-----KTRRWG--RKPMVAG- 107
sp|Q805D5|ANFC2_TAKRU      -----GSEG-GSRFLLDFLQQQS-----KTTRRG--RSSMVGG- 111
sp|Q76KW6|ANFC_ACITR      LEAEPPAENKPRRRLKDFMSSR-----KMFRGR--TKMKQQG- 131
sp|Q61839|ANFC_MOUSE      VDTKSR---AAWARLLHEHPN-----ARKYKG--GNKKGLS- 107
tr|Q544K5|Q544K5_MOUSE    VDTKSR---AAWARLLHEHPN-----ARKYKG--GNKKGLS- 107
tr|Q8VHG9|Q8VHG9_NOTAL    VDTKSR---AAWARLLHEHPN-----ARKNKG--GNKKGLS- 128
sp|P55207|ANFC_RAT        VDTKSR---AAWARLLHEHPN-----ARKYKG--GNKKGLS- 107
sp|P55206|ANFC_BOVIN      VDTKSR---AAWTRLLEHPN-----ARKYKG--GNKKGLS- 107
sp|P56283|ANFC_SHEEP      VDTKSR---AAWTRLLEHPN-----ARKYKG--GNKKGLS- 107
sp|P18104|ANFC_PIG        VDTKSR---AAWARLLHEHPN-----ARKYKG--GNKKGLS- 107
sp|P23582|ANFC_HUMAN      VDTKSR---AAWARLLQEHNP-----ARKYKG--ANKKGLS- 107
sp|P84715|ANF39_ORNAN     LDTRSRSRGRGVWTRLHDHPN-----PRKYKP--ANKKGLS- 102
tr|Q9QZ96|Q9QZ96_CAVPO    -----N-----ARKYKG--GNKKGLS- 14
sp|Q80017|ANFC4_ORYLA     VDTRAR---GMWARLLNDQPA-----SRRHKS--GSKKGGST 100
sp|Q805D3|ANFC4_TAKRU     MDTRAR---GVWARLLNDQPV-----PRRHKT--GIKKGGS- 99
tr|C1BXI5|C1BXI5_ESOLU    MDTRAK---GMWARLLNDQPN-----ARRHKQ--NSKKGTV- 99
tr|D2KXA5|D2KXA5_ANGJA    LNTRAR---GMWSRIMNDQPA-----SRKQKT--GVKKGAST 98
tr|Q1XGY7|Q1XGY7_ACTI     LDIRAK---AAWARLLNDHPN-----PRKSKG--INKKGLS- 99
sp|P40756|ANFD_RANCA      ADTRSR---AAWTRLNEHPN-----SRKIKG--INKKGTs- 99
sp|P0C7P5|BNP_TRIFL      TDGKQERQKWG---RMVQPDHHAAPGGGGGGGGG--ARRMKG--LAKKAMG- 174
sp|P0C7P6|BNP_TRIGA      ADGKQARQKWG---RMVQPDHHAAPGGGGGGGGG--ARRLKG--LAKKAVG- 191
sp|Q6LEM5|BNP1_BOTJA      PDGKQARQNWG---RMAHHDHHAAGGGGGGGGG--ARRLKG--LAKKGAA- 237
sp|Q9PW56|BNP2_BOTJA      PDGKQARQNWG---RMVHHDHHAAGGGGGGGGG--ARRLKG--LAKKGAA- 246
sp|P68515|BNP_BOTIN      PDGKQARQNWG---RMVHHDHHAAGGGGGGGGG--ARRLKG--LAKKGAA- 246
sp|Q90Y12|BNP_CRODU      TDGKQARQNWG---RLVSPDHHSAGGGGGGGGG--ARRLKG--LAKKRAG- 162
sp|Q2PE51|BNP_CRODO      TDGKQARQNWG---RLVSPDHHSAGGGGGGGGG--ARRLKG--LAKKRAG- 162
sp|B0VXV8|BNP_SISCA      TDGKQARQNWG---RMLNPDHHSAPGGGGGGGG--ARRLKG--LAKKRAG- 182
sp|Q27J49|BNP_LACMU      TDGKQARQNWG---RMMNPDHHAAGGGGGGG--GGGG--ARRLKG--LAKKRVG- 220
sp|P01021|BNP_AKGHA      TDGKQARQNWA---RMVNPDHHAAGGGGGGGGG--ARRLKG--LVKKGVA- 244
sp|Q09GK2|VNP_PHIOL      PDSKQARAAGW---RMVHPEHHAGGGGGGGGG--ARRLKG--LAKKGLG- 145
tr|D1MZV3|D1MZV3_RHATT    PDGKQSRAAWG---RMVHPEHHAGGGGGGGGG--ARRLKG--LPKKGLG- 142
tr|Q7T1M4|Q7T1M4_BOTJR    QAGAAELGPDGAPRPPRPPRSGRRAAAAAAERGARRLKG--LAKKGAA- 202
tr|Q402A2|Q402A2_PETMA    EGGSQVSG-GVWQRLFNDFVSN-----QRRFRG--RTKKKGK- 99
tr|Q402A3|Q402A3_LAMJA    EGGSQVSG-GVWQRLFNDFVSN-----QRRFRG--RTKKKGK- 131
tr|Q402A1|Q402A1_9PETR    -GGSQVSG-EVWQRLFNDFVSN-----QRRFRG--RTKKKGK- 116
sp|P21805|ANFC_CHICK      -----GLS- 3
tr|A9CDT6|A9CDT6_CHICK    QPASTSTADSDVQRILSDLLGL-----PQRYQN--RSKKGLS- 111
sp|P20968|ANFC_RANCA      QGDSPHVNEMTLQQLLNDPVG-----SRRYRQ--RNKKGYS- 110
sp|P55208|ANFC_TRISC      IGGRPFRQEAVLARLLKDLN-----PLRFRG--RSKKGPS- 117
sp|P23259|ANFC_SCYCA      IGGRPFRQEAVLARLLKDLN-----PLRFRG--RSKKGPS- 96
sp|P41319|ANFC_SQUAC      IGGRSFRQHDGLLRLLKDLN-----PLRFKG--RSKKGPS- 116
tr|Q2MH72|Q2MH72_9CHON    IASR-----PILARILKDLN-----PLRFRG--RSKKGPS- 112
tr|Q2MH73|Q2MH73_9CHON    IASR-----PILARILKDLN-----PLRFRG--RSKKGPS- 112
tr|Q2MH71|Q2MH71_9CHON    IASR-----PILARILKDLN-----PLRFRG--RSKKGPS- 112
tr|Q2MH74|Q2MH74_DASAK    IASR-----PILARILKDLN-----PLRFRG--RSKKGPS- 112
tr|Q2PF87|Q2PF87_CALMI    IGGRSFQHDGLLRLLKDLTIS-----PLRFNG--RSKKGPS- 120
sp|Q80018|ANFC3_ORYLA     SSSREAADESALTRLFADLLRT-----SKRSWG--RYKKGGM- 93
tr|Q4ADV1|Q4ADV1_ORYLA    SSSREAADESALTRLFADLLRT-----SKRSWG--RYKKGGM- 93
sp|Q805D4|ANFC3_TAKRU     SSTWALQKDDVLMRLFKDLLRT-----SKRSRS--RYKKGGL- 139
tr|C0H7B0|C0H7B0_SALSA    --NSALTGKEDVIARLLNDIMTT-----PKRSWS--RFKKGGL- 109
tr|C1BWD1|C1BWD1_ESOLU    --SALTGENAVARLLSDIMTT-----PKRSWG--RFKKGGM- 107
tr|D2KXA3|D2KXA3_ANGJA    -DAALSSNENALVRLNDILSS-----SKRSWS--RFKKGGL- 109
tr|B3DJJ2|B3DJJ2_DANRE    -NSALAGKYGMFERLLGDLST-----SKRSWS--RFKKGDL- 109
tr|Q1XGY8|Q1XGY8_ACTI     -QHRQAAHSSRMILKLDILTS-----SGRSWD--REKKSGL- 111
sp|Q8AXR2|ANFC2_ONCMY     ADIP-AQGDSTWLRLKGTLAN-----QKRAVT--DRSRRGWN- 112
sp|Q8AXR3|ANFC1_ONCMY     ADIP-AQGDSTWLRLKGTLAN-----QKRAVM--DRSRRGWN- 112
tr|C1BKS8|C1BKS8_OSMO     ADLPAAQEDSAWLRLKAALAN-----QKRAEP--DRSRRAWN- 113
tr|Q805E7|Q805E7_OREMO     ADAQTQPE-TPWLRLKLGALAN-----QKRAEP--DRSRRGWN- 112
tr|C3KH23|C3KH23_ANOFI     ADAQTQAE-TPWLRLKLGAVAN-----QKRAEP--DRSRRGWN- 112
sp|Q8AYR6|ANFC1_ORYLA     ADLQTQPE-TPWFLRLKALTN-----QKRAEP--DRSRRGWN- 112
sp|Q805D6|ANFC1_TAKRU     AEAD----TPWLRLRGALAN-----QKRAEP--DRSRRGWN- 107
sp|P18145|ANFC_ANGJA      VDVPSOND-NTWFRLRGALAN-----RKRALP--DRAKRGWN- 112
tr|Q1XGY9|Q1XGY9_ACTI     GDEPPANE-NALYLLLRRAAAN-----RTWISA--DRVKKAWS- 121
tr|A9CDT5|A9CDT5_CHICK    -----AAHPLLWRKALAS-----RKRALSGDWAOKAVP- 104

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FIG. 15G

Multiple Alignment of C-Type Natriuretic Peptides from Various Species

sp Q8AYR5 ANFC2_ORYLA	---GG	CFGMKMDRIGSISGLGC	126 (SEQ ID NO: 31)
sp Q805D5 ANFC2_TAKRU	---RG	CFGMKIDRIGSISGLGC	130 (SEQ ID NO: 32)
sp Q76KW6 ANFC_ACITR	---RG	CFGMKLDRIIGSMSGLGC	150 (SEQ ID NO: 33)
sp Q61839 ANFC_MOUSE	---KG	CFGLKLDRIIGSMSGLGC	126 (SEQ ID NO: 34)
tr Q544K5 Q544K5_MOUSE	---KG	CFGLKLDRIIGSMSGLGC	126 (SEQ ID NO: 35)
tr Q8VHG9 Q8VHG9_NOTAL	---KG	CFGLKLDRIIGSMSGLGC	147 (SEQ ID NO: 36)
sp P55207 ANFC_RAT	---KG	CFGLKLDRIIGSMSGLGC	126 (SEQ ID NO: 37)
sp P55206 ANFC_BOVIN	---KG	CFGLKLDRIIGSMSGLGC	126 (SEQ ID NO: 38)
sp P56283 ANFC_SHEEP	---KG	CFGLKLDRIIGSMSGLGC	126 (SEQ ID NO: 39)
sp P18104 ANFC_PIG	---KG	CFGLKLDRIIGSMSGLGC	126 (SEQ ID NO: 40)
sp P23582 ANFC_HUMAN	---KG	CFGLKLDRIIGSMSGLGC	126 (SEQ ID NO: 41)
sp P84715 ANF39_ORNAN	---KG	CFGLKLDRIIGSTSLGC	121 (SEQ ID NO: 42)
tr Q9QZ96 Q9QZ96_CAVPO	---KG	CFGLKLDRIIGSMSGLGC	33 (SEQ ID NO: 43)
sp Q80017 ANFC4_ORYLA	-SRSG	CFGHKMDRIGTISGMGC	121 (SEQ ID NO: 44)
sp Q805D3 ANFC4_TAKRU	-SRSG	CFGHKMDRIGTISGMGC	120 (SEQ ID NO: 45)
tr C1BXI5 C1BXI5_ESOLU	-PRSG	CFGQKLDRIIGTSLGMGC	121 (SEQ ID NO: 46)
tr D2KXA5 D2KXA5_ANGJA	PARGG	CFGHKLDRIISTLSGMGC	120 (SEQ ID NO: 47)
tr Q1XGY7 Q1XGY7_9ACTI	---KG	CFGLKLDRIIGSMSGLGC	118 (SEQ ID NO: 48)
sp P40756 ANFD_RANCA	---KG	CFGLKLDRIIGAMSGLGC	118 (SEQ ID NO: 49)
sp P0C7P5 BNP_TRIFL	---KG	CFGHKLDRIIGSTSLGC	193 (SEQ ID NO: 50)
sp P0C7P6 BNP_TRIGA	---KG	CFGLPLDRIIGSMSGMGC	210 (SEQ ID NO: 51)
sp Q6LEM5 BNP1_BOTJA	---KG	CFGLKLDRIIGTMSGLGC	256 (SEQ ID NO: 52)
sp Q9PW56 BNP2_BOTJA	---KG	CFGLKVDRIIGTMSGLGC	265 (SEQ ID NO: 53)
sp P68515 BNP_BOTIN	---KG	CFGLKLDRIIGTMSGLGC	265 (SEQ ID NO: 54)
sp Q90Y12 BNP_CRODU	---NG	CFGLKLDRIIGSMSGLGC	181 (SEQ ID NO: 55)
sp Q2PE51 BNP_CRODO	---NG	CFGLKLDRIIGSMSGLGC	181 (SEQ ID NO: 56)
sp B0VXV8 BNP_SISCA	---SG	CFGLKLDRIIGSMSGLGC	201 (SEQ ID NO: 57)
sp Q27J49 BNP_LACMU	---DG	CFGLKLDRIIGSMSGLGC	239 (SEQ ID NO: 58)
sp P01021 BNP_AKHA	---KG	CFGLKLDRIIGTMSGLGC	263 (SEQ ID NO: 59)
sp Q09GK2 VNP_PHIOL	---KG	CFGLKLDRIIGSMSGLGC	164 (SEQ ID NO: 60)
tr D1MZV3 D1MZV3_RHATT	---SG	CFGLKLDRIIGSMSGLGC	161 (SEQ ID NO: 61)
tr Q7T1M4 Q7T1M4_BOTJR	---KG	CFGLKLDRIIGTMSGLGC	221 (SEQ ID NO: 62)
tr Q402A2 Q402A2_PETMA	----	CFGVKLDRIIGSMSGLGC	116 (SEQ ID NO: 63)
tr Q402A3 Q402A3_LAMJA	----	CFGVKLDRIIGSMSGLGC	148 (SEQ ID NO: 64)
tr Q402A1 Q402A1_9PETR	----	CFGVKLDRIIGSMSGLGC	133 (SEQ ID NO: 65)
sp P21805 ANFC_CHICK	---RS	CFGVKLDRIIGSMSGLGC	22 (SEQ ID NO: 66)
tr A9CDT6 A9CDT6_CHICK	---RS	CFGVKLDRIIGSMSGLGC	130 (SEQ ID NO: 67)
sp P20968 ANFC_RANCA	---RG	CFGVKLDRIIGAFSGLGC	129 (SEQ ID NO: 68)
sp P55208 ANFC_TRISC	---RG	CFGVKLDRIIGAMSGLGC	136 (SEQ ID NO: 69)
sp P23259 ANFC_SCYCA	---RG	CFGVKLDRIIGAMSGLGC	115 (SEQ ID NO: 70)
sp P41319 ANFC_SQUAC	---RS	CFGLKLDRIIGAMSGLGC	135 (SEQ ID NO: 71)
tr Q2MH72 Q2MH72_9CHON	---RG	CFGVKLDRIIGAMSGLGC	131 (SEQ ID NO: 72)
tr Q2MH73 Q2MH73_9CHON	---RG	CFGVKLDRIIGAMSGLGC	131 (SEQ ID NO: 73)
tr Q2MH71 Q2MH71_9CHON	---RG	CFGVKLDRIIGAMSGLGC	131 (SEQ ID NO: 74)
tr Q2MH74 Q2MH74_DASAK	---RG	CFGVKLDRIIGAMSGLGC	131 (SEQ ID NO: 75)
tr Q2PF87 Q2PF87_CALMI	---RG	CFGVKLDRIIGAMSGLGC	139 (SEQ ID NO: 76)
sp Q80018 ANFC3_ORYLA	---RS	CFGVRLERIGSFSGGLGC	112 (SEQ ID NO: 77)
tr Q4ADV1 Q4ADV1_ORYLA	---RS	CFGVRLERIGSFSGGLGC	112 (SEQ ID NO: 78)
sp Q805D4 ANFC3_TAKRU	---RS	CFGVRLARIGSFSGGLGC	158 (SEQ ID NO: 79)
tr C0H7B0 C0H7B0_SALSA	---RS	CFGVRLERIGSFSGGLGC	128 (SEQ ID NO: 80)
tr C1BWD1 C1BWD1_ESOLU	---RS	CFGVRLERIGSFSGGLGC	126 (SEQ ID NO: 81)
tr D2KXA3 D2KXA3_ANGJA	---RS	CFGVRLERIGSFSGGLGC	128 (SEQ ID NO: 82)
tr B3DJJ2 B3DJJ2_DANRE	---RS	CFGVRLERIGSFSGGLGC	128 (SEQ ID NO: 83)
tr Q1XGY8 Q1XGY8_9ACTI	---RS	CFGVRLDRIIGSMSGLGC	130 (SEQ ID NO: 84)
sp Q8AXR2 ANFC2_ONCMY	---RG	CFGLKLDRIIGSMSGLGC	131 (SEQ ID NO: 85)
sp Q8AXR3 ANFC1_ONCMY	---RG	CFGLKLDRIIGSMSGLGC	131 (SEQ ID NO: 86)
tr C1BKS8 C1BKS8_OSMMO	---RG	CFGLKLDRIIGSMSGLGC	132 (SEQ ID NO: 87)
tr Q805E7 Q805E7_OREMO	---RG	CFGLKLDRIIGSMSGLGC	131 (SEQ ID NO: 88)
tr C3KH23 C3KH23_ANOFI	---RG	CFGLKLDRIIGSMSGLGC	131 (SEQ ID NO: 89)
sp Q8AYR6 ANFC1_ORYLA	---RG	CFGLKLDRIIGSMSGLGC	131 (SEQ ID NO: 90)
sp Q805D6 ANFC1_TAKRU	---RG	CFGLKLDRIIGSMSGLGC	126 (SEQ ID NO: 91)
sp P18145 ANFC_ANGJA	---RG	CFGLKLDRIIGSLSGGLGC	131 (SEQ ID NO: 92)
tr Q1XGY9 Q1XGY9_9ACTI	---KG	CFGLKLDRIIGSISGLGC	140 (SEQ ID NO: 93)
tr A9CDT5 A9CDT5_CHICK	---RG	CFGLKMDRIIGAFSGLGC	123 (SEQ ID NO: 94)
CONSENSUS SEQUENCE	*** : ** : ** : **	CFGXXXXRXXXXSGXGC	(SEQ ID NO: 95)

FIG. 16
Schematic Structure of Natriuretic Peptide



Schematic Structures of Exemplary Fc-NP or NP-Fc Fusion Proteins

FIG. 17A

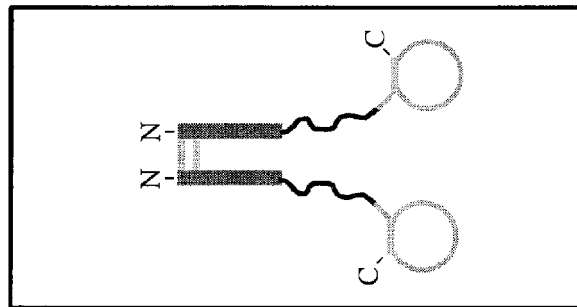


FIG. 17B

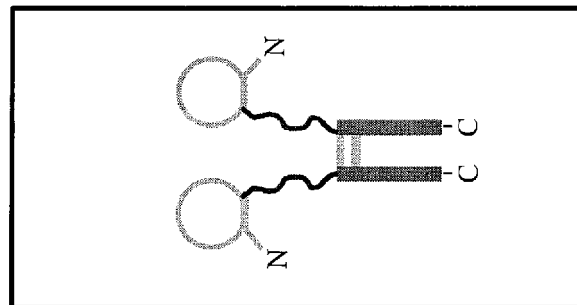


FIG. 17C

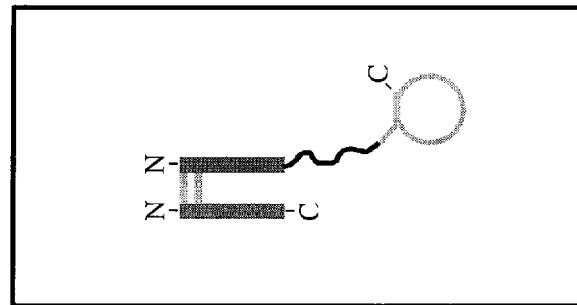


FIG. 17D

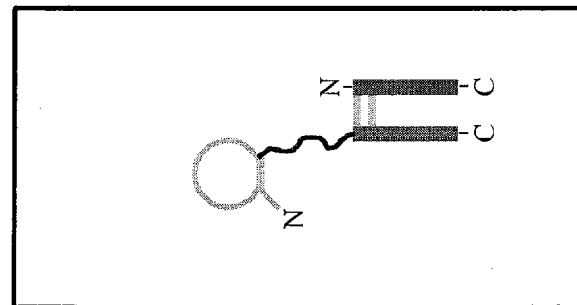


FIG. 17E

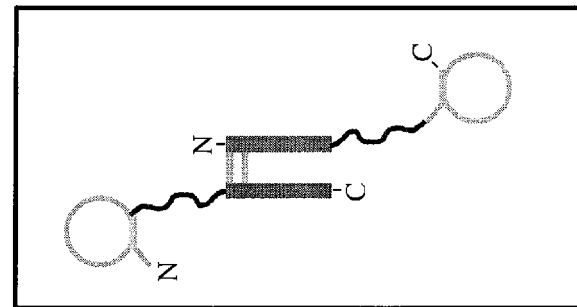


FIG. 18A

NC2st Protein Sequence (With Signal Sequence)

Sequence:

10 20 30 40 50 60
MGVHECPAWL WLLLSLLSLW PGAYAAWSH PQFEQSGGG GENLYFQGGD KTHTCPPCPA

70 80 90 100 110 120
PELLGGPSVF LFPPKPKDTL MISRTPEVC VVDVSHEDP EVKFNWYVDG VEVHNAKTKP

130 140 150 160 170 180
REEQYNSTYR VVSVLTVLHQ DWLNGKEYKC KVSNKALPAP IEKTISKAKG QPREPQVYTL

190 200 210 220 230 240
PPSREEMTKN QVSLTCLVKG FYPSDIAVEW ESNQGPENNY KTTPPVLDSD GSFFLYSKLT

250 260 270 280 290 300
VDKSRWQQGN VFSCSVMHEA LHNHYTQKSL SLSPGKGGG SGGGSGGGG SGLSKGCFG

310
LKLDRIQSMG GLGC

(SED ID NO: 501)

Number of amino acids: 314
Molecular weight of monomer: 34053.5

1-25 = Signal peptide
26-27 = Linker
28-35 = Strep-tag II
36-41 = Linker
42-47 = Tobacco etch virus protease cleavage sequence
48-49 = Linker
50-276 = Fc domain of human IgG1
277-292 = Glycine-rich linker
293-314 = C-type natriuretic peptide

FIG. 18B**NC2st Protein Sequence (Without Signal Sequence)**

NC2st (w/o sig. seq.) ASWSHPQFEQSGGGGGENLYFQGGDKTHTCPPCPAPELLGGPSVFLFPPKPD~~TL~~MISRTPEVTCVVVDVSHE
DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP~~IE~~KTISKAKGQ
PREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK~~TT~~PPVLDSDGSFFLYSKLTVDKS
RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGGSGGGSGGLSKGCFGLKLD~~RIGSM~~SGGLGC
(SEQ ID NO: 502)

FIG. 18C

NC2st DNA Sequence

ATGGGCGTGACGAGTGTCTGCTGGCTGTGGCTGCTGTGAGCCTGCTGTCTCTGTGGCCTGGCGCCTACGCCGCTCTTTGGAGC
CACCCCCAGTTTGAGCAGTCTGGCGGAGGAGGCGAGAACCTGTACTTTCAGGGCGGCGACAAGACCCACACCTGTCCCCCTTGT
CCTGCCCCCTGAGCTGCTGGGCGGACCCAGCGTGTTCCTGTTCCCCCAAGCCCAAGGACACCCCTGATGATCAGCCGGACCCCCGAA
GTGACCTGCGTGGTGGTGGACGTGTCCACGAGGACCCCTGAAGTGAAGTTCAATTGTACGTGGACGGCGTGGAGGTGCACAACGCC
AAGACCAAGCCCCGGGAGGAACAGTACAACAGCACCTACCGGGTGGTGTCCGTGCTGACCGTGTGCACCCAGGACTGGCTGAACGGC
AAAGAGTACAAGTGCAAGTCTCCAACAAGGCCCTGCCTGCCCCCATCGAGAAAACCATCAGCAAGGCCAAGGCCAGCCAGAGAA
CCCCAGGTGTACACCCCTGCCCCCGAGCGGAGGAAATGACCAAGAACCCAGGTGTCCCTGACCTGCCTGGTGAAGGGCTTCTACCCC
AGCGATATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCTGAGAACAACTACAAGACCAACCCCCCTGTGCTGGACAGCGACGGAAGC
TTCCTCCTGTACTCCAACTGACCGTGGACAAGCCGGTGGCAGCAGGCAACGTGTTTCACTGACGTGACGTGATGCACGAGGCCCTG
CACAAACCACTACACCCAGAAGTCCCTGAGCCTGTCTCCTGGCAAGGGCGGAGGGGGAAGTGGAGCGGAGGAAGCGGGGAGGCGGGA
AGCGGCGGACTGAGCAAGGGCTGCTTCGGCCCTGAAGCTGGACCCGGATCGGCAGCATGAGCGGCCCTGGGCTGCTGA (SEQ ID NO:
801)

FIG. 19A
NC2B Protein Sequences

NC2B (w/sig. seq.)	MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTTLPSSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGLSKGCGFLKLDRI GMSGLGC (SEQ ID NO: 503)
NC2B (w/o sig. seq.)	DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTTLPSSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGGSFFLYSKLTVDKSRWQGNVSCSVMHEALHNHYTQK SLSLSPGKGGGGGGGGGGGGGGLSKGCGFLKLDRI GMSGLGC (SEQ ID NO: 504)
D10-NC2 (w/sig. seq.)	MGVHECPAWLWLLLSLLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTISKAKGQPREPQVYTTLPSSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGSF FLYSKLTVDKSRWQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGLSKGCGFLKLDRI GMSGLGC (SEQ ID NO: 607)
D10-NC2 (w/o sig. seq.)	DDDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTTLPSSRE EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGGSFFLYSKLTVDKSRWQGNVSCSVMH EALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGLSKGCGFLKLDRI GMSGLGC (SEQ ID NO: 608)

FIG. 19B
NC2B DNA Sequence

ATGGGCGTGCAAGAGTGTCTGCTGGCTGTGGCTGTGCTGAGCCTGTCTCTGTGGCCTGGCGCCTACGCCGACAAAGACCCAC
ACCTGTCCCCCTTGCTGCCCCCTGAGCTGTCTGGCGGACCCAGCGTGTTCCTGTTCCCCCAAGCCCAAGGACACCCCTGATGATC
AGCCGGACCCCCGAAGTGACCTGCGTGGTGGTGGACGTGTCCCACAGGACCCCTGAAGTGAAGTTCAATTGGTACGTGGACGGCGTG
GAGGTGCACAAACGCCAAGACCAAGCCCCGGGAGGAACAGTACAACAGCACCTACCCGGTGGTGTCCGTGCTGACCGTGTGCACCCAG
GACTGGCTGAACGGCAAAGAGTACAAGTGCAAGGTCTCCAACAAGGCCCTGCCCTGCCCCCATCGAGAAAACCATCAGCAAAGGCCAAG
GGCAGCCCCAGAACCCAGGTGTACCCCTGCCCCCAGCCGGGAGGAAATGACCAAGAACCCAGGTGTCCCTGACCTGCTGCTGGTG
AAGGGCTTCTACCCCAAGCGATATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCTGAGAACAACTACAAAGACCCACCCCTGTGCTG
GACAGCGACGGCAGCTTCTTCCTGTACTCCAACCTGACCCGTGGACAAGAGCCGGTGGCAGCAGGGCAACGTGTTTCAGCTGCAGCGTG
ATGCACGAGGCCCTGCACAACCACTACACCCAGAAATCCCTGAGCCTGTCTCCTGGCAAGGCGGAGGGGGAAGTGGAGCGGGAGGA
AGCGGGGAGGCGGAAGCGCGGACTGAGCAAGGGTGTCTTCGGCCTGAAGCTGGACCGGATCGGCAGCATGAGCGGCCCTGGGCTGC
TGA (SEQ ID NO: 802)

NC2B-34
(w/o sig. seq.)

[illegible]

FIG. 20B
NC2B-22 DNA Sequence

ATGGGCGTGCAAGAGTGTCTGCTGGCTGTGGCTGTGCTGAGCCTGTCTCTGTGGCCTGGCGCCTACGCCGACAAAGACCCAC
ACCTGTCCCCCTTGTCCTGCCCTGAGCTGCTGGCGGACCCAGCGTGTTCCTGTTCCCCCAAGCCCAAGGACACCCCTGATGATC
AGCCGGACCCCCGAAGTGACCTGCGTGGTGGTGTCCACAGGACCCCTGAAGTGAAGTTCAATTGGTACGTGGACGGCGTG
GAGGTGCACAAACGCCAAGACCAAGCCCCGGGAGAACAGTACAACAGCACCTACCGGGTGGTGTCCGTGCTGACCGTGTGCACCCAG
GACTGGCTGAACGGCAAAGAGTACAAGTGCAAGGTCTCCAACAAGGCCCTGCCCTGCCCCCATCGAGAAAACCATCAGCAAAGGCCAAG
GGCAGCCCCAGAACCCAGGTGTACCCCTGCCCCCCAGCCGGGAGGAAATGACCAAGAACCCAGGTGTCCCTGACCTGCTGCTGGTG
AAGGGCTTCTACCCCAAGCGATATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCTGAGAACAACTACAAAGACCCACCCCTGTGCTG
GACAGCGACGGCAGCTTCTTCCTGTACTCCAACCTGACCCGTGGACAAGAGCCCGTGGCAGCAGGGCAACGTGTTTCAGCTGCAGCGTG
ATGCACGAGGCCCTGCACAACCACTACACCCAGAGTCCCTGAGCCTGTCTCCTGGCAAGGCGGAGGGGGAAGTGGAGCGGGAGGA
AGCGGGGAGGCGGAAGCGGAGCGGAGGATCTGGCGGCGGACTGAGCAAGGGCTGCTTCGGCCTGAAGCTGGACCGGATCGGCAGC
ATGAGCGGCCCTGGGCTGCTGA (SEQ ID NO: 803)

FIG. 20C
NC2B-28 DNA Sequence

ATGGGCGTGCAAGAGTGTCCTGCCTGGCTGTGGCTGCTGTGAGCCCTGCTGTCTCTGTGGCCCTACGCCGACAAAGACCCAC
ACCTGTCCCCCTTGTCCTGCCCTGAGCTGCTGGCGGACCCAGCGTGTTCCCTGTTCCCCCAAGCCCAAGGACACCCCTGATGATC
AGCCGGACCCCCGAAGTGACCTGCGTGGTGGACGTGTCCACAGGACCCCTGAAGTCAATTGGTACGTGGACGGCGTG
GAGGTGCACAACGCCAAGACCAAGCCCCGGGAGGAACAGTACAACAGCACCTACCCGGTGGTGTCCGTGCTGACCGTGTGCACCCAG
GACTGGCTGAACGGCAAAGAGTACAAGTGCAAGGTCTCCAACAAGGCCCTGCCCTGCCCCCATCGAGAAAACCATCAGCAAAGGCCAAG
GGCCAGCCAGAGAACCCAGGTGTACCCCTGCCCCCAAGCCGGGAGGAAATGACCAAGAACCAAGGTGTCCCTGACCTGCTGGTG
AAGGGCTTCTACCCCAAGCGATATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCCTGAGAACAACTACAAAGACCCACCCCTGTGCTG
GACAGCGACGGCAGCTTCTTCCGTACTCCAACCTGACCGTGGACAAGAGCCGGTGGCAGCAGGGCAACGTGTTCAAGCTGCAGCGTG
ATGCACGAGGCCCTGCACAACCACTACACCCAGAGTCCCTGAGCCTGTCTCCTGGCAAGGCGGAGGGGGAAGTGGAGCGGGAGGA
AGCGGGGAGGCGGAAGCGGAGCGGAGGATCTGGCGGCGGAGGAAGTGGCGGAGGCGGACTGAGCAAAGGGCTGCTTCGGCCTGAAG
CTGGACCCGGATCGGCAGCATGAGCGGCCCTGGGGCTGCTGA (SEQ ID NO: 804)

FIG. 20D
NC2B-34 DNA Sequence

ATGGGCGTGCAAGAGTGTCCTGCCTGGCTGTGGCTGCTGTGAGCCCTGCTGTCTCTGTGGCCCTACGCCGACAAAGACCCAC
ACCTGTCCCCCTTGTCCTGCCCTGAGCTGCTGGCGGACCCAGCGTGTTCCCTGTTCCCCCAAGCCCAAGGACACCCCTGATGATC
AGCCGGACCCCCGAAGTGACCTGCGTGGTGGACGTGTCCACAGGACCCCTGAAGTGAAGTTCAATTGGTACGTGGACGGCGTG
GAGGTGCACAAACGCCAAGACCAAGCCCCGGGAGGAACAGTACAACAGCACCTACCGGGTGGTGTCCGTGCTGACCGTGTGCACCCAG
GACTGGCTGAACGGCAAAGAGTACAAGTGCAAGGTCTCCAACAAGGCCCTGCCCTGCCCCCATCGAGAAAACCATCAGCAAAGGCCAAG
GGCCAGCCAGAGAACCCAGGTGTACCCCTGCCCCCAAGCCGGGAGGAAATGACCAAGAACCAAGGTGTCCCTGACCTGCCCTGGTG
AAGGGCTTCTACCCCAAGCGATATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCCTGAGAACAACTACAAAGACCCACCCCTGTGCTG
GACAGCGACGGCAGCTTCTTCCTGTACTCCAACCTGACCCGTGGACAAGAGCCCGGTGGCAGCAGGGCAACGTGTTTCAGCTGCAGCGTG
ATGCACGAGGCCCTGCACAACCACTACACCCAGAGTCCCTGAGCCTGTCTCCTGGCAAGGCGGAGGGGGAAGTGGAGCGGGAGGA
AGCGGGGAGGCGGAAGCGGAGCGGAGGATCTGGCGGCGGAGGAAGTGGCGGAGGCGGAGCGGCGGAGGGGAGGACTGAGCAAG
GGCTGCTTCGGCCCTGAAGCTGGACCCGGATCGGCAGCATGAGCGGCCCTGGGCTGCTGA (SEQ ID NO: 805)

FIG. 21

NC2 Variants

NC2-KGANKK
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGSPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQOQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGGSGKANKKGLSKGCGGLKLDRI GSMGLGC
(SEQ ID NO: 511)

NC2-KGANKK
(w/o sig. seq.)

DKTHTCPPCPAPELLGSPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQK
SLSLSPGKGGGGSGGGSGKANKKGLSKGCGGLKLDRI GSMGLGC (SEQ ID NO: 512)

NC2-KGANQK
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGSPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQOQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGGSGKANQKGLSKGCGGLKLDRI GSMGLGC
(SEQ ID NO: 513)

NC2-KGANQK
(w/o sig. seq.)

DKTHTCPPCPAPELLGSPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQK
SLSLSPGKGGGGSGGGSGKANQKGLSKGCGGLKLDRI GSMGLGC (SEQ ID NO: 514)

FIG. 22

NC2 Variants

NC2-CNP53mut2
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGSVFLFPPKPKDTLMI SRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTTLPSSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKGC
FGILKLDRI GSMGLGC (SEQ ID NO: 515)

NC2-CNP53mut2
(w/o sig. seq.)

DKTHTCPPCPAPELLGGSVFLFPPKPKDTLMI SRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTTLPSSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQK
SLSLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKGCGFGLKLDRI GSMGLGC (SEQ ID
NO: 516)

FIG. 23

Fc-CNP53 Constructs

Fc-CNP53-A
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSRREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQOGNVFSCSMHEALHNHYTQKSLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANKGLSKGC
EGLKLDRIGSASGLGC (SEQ ID NO: 517)

Fc-CNP53-A
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQK
SLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANKGLSKGCGFLKLDRIGSASGLGC (SEQ ID
NO: 518)

Fc-CNP53-AAA
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYTLPPSRREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQOGNVFSCSMHEALHNHYTQKSLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANAAGLSKGC
EGLKLDRIGSASGLGC (SEQ ID NO: 519)

Fc-CNP53-AAA
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQK
SLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANAAGLSKGCGFLKLDRIGSASGLGC (SEQ ID
NO: 520)

FIG. 24
NP Multiple Sequence Alignment and CDNP Constructs

Human ANP	SLRRSSCFGGRMDRIGAQSGLGNCNSFRY	(SEQ ID NO: 1)
Rat ANP	SLRRSSCFGGRIDRIGAQSGLGNCNSFRY	(SEQ ID NO: 96)
Urodilatin	TAPRSLRRSSCFGGRMDRIGAQSGLGNCNSFRY	(SEQ ID NO: 2)
Human BNP	SPKMVQSGGCFGRKMDRISSSSSGLGCKVLRRH	(SEQ ID NO: 3)
Rat BNP	SQDSAFRIQERLRNSKMAHSSSSCFGQKIDRIGAVSRGLGCDGLRLF	(SEQ ID NO: 97)
Pig BNP	SPKTMRDSSGCFGRRIDRIGSLGGLGNCVLRRY	(SEQ ID NO: 98)
DNP	EVKYDPFCFCHKIDRINHVSNLGCPSLRDRPNAPSTSA	(SEQ ID NO: 5)
TNP-C	SDSKIENGCGFGFPLDRIGSVGLGNCNRIQNPPKFSGE	(SEQ ID NO: 99)
CDNP	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCPSLRDRPNAPSTSA ^{::}	(SEQ ID NO: 100)
CDNP-N1 (C7)	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGNCNSLRDRPNAPSTSA	(SEQ ID NO: 101)
CDNP-G1 (C8)	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCGSLRDRPNAPSTSA	(SEQ ID NO: 102)
CDNP-H1 (C9)	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCHSLRDRPNAPSTSA	(SEQ ID NO: 103)
CDNP-K1	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCKSLRDRPNAPSTSA	(SEQ ID NO: 104)
CDNP-Z1 (Z=hydroxyproline)	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCSLRDRPNAPSTSA	(SEQ ID NO: 105)
CDNP-S3	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCPSSRDRPNAPSTSA	(SEQ ID NO: 106)
CDNP-A4	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCPSLADPRNAPSTSA	(SEQ ID NO: 107)
CDNP-A5	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCPSLRAPRNPAPSTSA	(SEQ ID NO: 108)
CDNP-S3A4 (C12)	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCPSSADPRNAPSTSA	(SEQ ID NO: 109)
CDNP-A4A5	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCPSLAAPRNPAPSTSA	(SEQ ID NO: 110)
CDNP-S3A5 (C11)	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCPSSRAPRNPAPSTSA	(SEQ ID NO: 111)
CDNP-(A17)S3A5	GLSKGCGFGLKLDRI ^{***} GSASGLGCPSSRAPRNPAPSTSA	(SEQ ID NO: 112)
CDNP-S3A4A5 (C10)	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCPSSAAPRNPAPSTSA	(SEQ ID NO: 113)
CDNP-(A17)S3A4A5	GLSKGCGFGLKLDRI ^{***} GSASGLGCPSSAAPRNPAPSTSA	(SEQ ID NO: 114)
CDNP-S3A4A5R6 (C13)	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCPSSAARRNPAPSTSA	(SEQ ID NO: 115)
CDNP-S3A4A5S7 (C14)	GLSKGCGFGLKLDRI ^{***} GSM ^{***} SGLGCPSSAAPSPNAPSTSA	(SEQ ID NO: 116)
DNP TAIL	PSLRDRPNAPSTSA	(SEQ ID NO: 117)
CONSENSUS SEQUENCE FOR DNP C-TERMINAL TAIL	XSXXXXPNAPSTSA	(SEQ ID NO: 118)

FIG. 25A

Exemplary Constructs Having N-terminal NP fused to C-terminal Fc Domain

CNP-16AAlinker-Fc-His₁₀
(NC1)
GLSKGCFGLKLDRI¹GSM²SLGCGGGGGGGGGGGGGGSGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGKGGENLYFQGSHHHHHHHHH (SEQ ID NO: 521)

CNP-6AAlinker-Fc-His₁₀
(NC3)
GLSKGCFGLKLDRI¹GSM²SLGCGGGGGGGGGGGGSGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGKGGENLYFQGSHHHHHHHHH (SEQ ID NO: 522)

CNP-6AAlinker-Fc
GLSKGCFGLKLDRI¹GSM²SLGCGGGGGGGGGGGGSGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 523)

CDNP-Fc
GLSKGCFGLKLDRI¹GSM²SLGCGPSLRDPRNAPST³ADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 524)

CDNP-A17saa-Fc
GLSKGCFGLKLDRI¹GSA²SLGCPSSA³APRPNAPST⁴ADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 525)

CDNP-A17sra-Fc
GLSKGCFGLKLDRI¹GSA²SLGCPSSRA³PRPNAPST⁴ADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 526)

FIG. 25B
NC1 DNA Sequence

ATGGGCGTGACGAGTGTCTGCTGGCTGTGGCTGTGCTGAGCCTGTCTGTGGCCCTGGCGCCTACGCCGGCCTGAGCAAAG
GGCTGCTTCGGCCTGAAGCTGGACCGGATCGGCAGCATGTCTGGCCTGGCTGTGGCGGAGGATCTGGCGGCGGAGAAAGTGGC
GGAGGGCAGCGGCGATAAGACCCACACCTGTCCCCCTTGTCTGCCCCTGAGCTGTGGGGGACCCAGCGTGTTCCTGTTCCTCC
CCAAAGCCCCAAGGACACCCCTGATGATCAGCCGGACCCCCGAAGTGACCTGCTGGTGGTGTGCCACGAGGACCCCTGAAGTG
AAGTTCAATTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAGACCAAGCCCCGGGAGGAACAGTACAACAGCACCTACCGGGTG
GTGTCCGTGCTGACCGTGTGCAACGAGGACTGGCTGAACGGCAAAAGATACAAGTGCAAGGTCTCCAACAAGGCCCTGCCCTGCCCCC
ATCGAGAAAACCATCAGCAAGGCCAAGGCCAGCCAGAGAACCCAGGTGTACACCCCTGCCCCAGCCGGAGGAAATGACCAAAG
AACCAGGTGTCCCTGACCTGCCCTGGTGAAGGGCTTCTACCCAGCGATATCGCCGTGGAGTGGGAGAGCAACGGCCAGCCTGAGAAC
AACTACAAGACCACCCCCTGTGTGTGACAGCGACGGCAGCTTCTTCCTGTACTCCAAACTGACCGTGGACAAAGAGCCGGTGGCAG
CAGGGCAACGTGTTTCAAGCTGCAGCGTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAAGTCCCTGAGCCTGTCTCTGGCAAAG
GGCGGCGAGAACCTGTACTTTCAGGGCAGCCACCACCATCACCATCATCACTGA (SEQ ID NO: 806)

FIG. 26
Human CNP22 and Point Mutations at Position 17

CNP22	GLSKGCFGLKLDRI ^{MS} GLGC	(SEQ ID NO: 4)
CNP-F17 (C15)	GLSKGCFGLKLDRI ^{GS} FSGLGC	(SEQ ID NO: 119)
CNP-L17 (C16)	GLSKGCFGLKLDRI ^{GS} <u>I</u> SGLGC	(SEQ ID NO: 120)
CNP-I17 (C17)	GLSKGCFGLKLDRI ^{GS} <u>I</u> SGLGC	(SEQ ID NO: 121)
CNP-T17 (C18)	GLSKGCFGLKLDRI ^{GS} <u>TS</u> GLGC	(SEQ ID NO: 122)
CNP-V17 (C19)	GLSKGCFGLKLDRI ^{GS} <u>V</u> SGLGC	(SEQ ID NO: 123)
CNP-A17 (C1)	GLSKGCFGLKLDRI ^{GS} <u>A</u> SGLGC	(SEQ ID NO: 124)
CNP-S17	GLSKGCFGLKLDRI ^{GS} <u>SS</u> GLGC	(SEQ ID NO: 125)
CNP-E17	GLSKGCFGLKLDRI ^{GS} <u>E</u> SGLGC	(SEQ ID NO: 156)
CNP-R17	GLSKGCFGLKLDRI ^{GS} <u>RS</u> GLGC	(SEQ ID NO: 157)
CNP-Y17	GLSKGCFGLKLDRI ^{GS} <u>Y</u> SGLGC	(SEQ ID NO: 158)
CONSENSUS:	GLSKGCFGLKLDRI ^{GS} <u>X</u> SGLGC	(SEQ ID NO: 126)

FIG. 28A
Additional CNP Variants

GDLRVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1001)
PDLRVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1002)
MDLRVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1003)
DLRVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1004)
LRVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1005)
RVDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1006)
VDTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1007)
DTKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1008)
TKSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1009)
KSRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1010)
SRAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1011)
RAAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1012)
AAWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1013)
AWARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1014)
WARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1015)
ARLLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1016)
RLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1017)
LLQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1018)
LQEHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1019)
EHPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1020)
HPNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1021)
PNARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1022)
NARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1023)
ARKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1024)
RKYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1025)
KYKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1026)
YKGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1027)
KGANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1028)
GANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1029)
ANKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1030)
NKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1031)

FIG. 28B

KKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1032)
KGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1033)
LSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1034)
SKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1035)
KGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1036)
GCFLKLDRI GSM SGLGC	(SEQ ID NO: 1037)
QEHPNARKYKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1038)
PQEHPNARKYKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1039)
MQEHPNARKYKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1040)
GQEHPNARKYKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1041)
GQEHPNARKYKGANKPKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1042)
GQEHPNARKYKGANKQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1043)
GQEHPNARKYKGANKQQLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1044)
GQEHPNARKYKGANKPGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1045)
GQEHPNARKYKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1046)
PGQEHPNARKYKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1047)
MGQEHPNARKYKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1048)
GANRRGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1049)
GANRRGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1050)
PGANRRGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1051)
MGANRRGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1052)
GHKSEVAHRFKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1053)
GHKSEVAHRFKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1054)
PGHKSEVAHRFKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1055)
MGHKSEVAHRFKGANKKKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1056)
RGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1057)
ERGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1058)
GANQQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1059)
GANRRGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1060)
GANPRGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1061)
GANSSGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1062)

FIG. 28C

	GANPRGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1063)
	GANRRGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1064)
	GANQQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1065)
	GANSSGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1066)
	AAWARLLQEHNPAGLSKCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1067)
	AAWARLLQEHPNARGLSKCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1068)
	DLRVDTKSRAAWARGLSKCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1069)
	GQEHNPARKYKGANPKGSLKCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1070)
	GQEHNPARKYKGANQKGLSKCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1071)
	GLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1072)
	ERGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1073)
	RGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1074)
	GLSRGCFGLRLDRI GSM SGLGC	(SEQ ID NO: 1075)
	GLSKGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1076)
	GLSKGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1077)
	RLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1078)
	ELSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1079)
	GLSKRCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1080)
	GLSKQCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1081)
	GLSKSCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1082)
	GLSKGCFGLKLDRI SSMSGLGC	(SEQ ID NO: 1083)
	GLSKGCFGLKLDRI NSMSGLGC	(SEQ ID NO: 1084)
	GLSKGCFGLKLDRI RSMSGLGC	(SEQ ID NO: 1085)
	GLSKGCFGLKLDRI XSMSGLGC	(SEQ ID NO: 1086)
	GLSKGCFGLKLDRI GSM SSLGC	(SEQ ID NO: 1087)
	GLSKGCFGLKLDRI GSM SRLGC	(SEQ ID NO: 1088)
	GLSKGCFGLKLDRI GSM SNLGC	(SEQ ID NO: 1089)
	GLSKGCFGLKLDRI GSM SGLSC	(SEQ ID NO: 1090)
	GLSKGCFGLKLDRI GSM SGLTC	(SEQ ID NO: 1091)
	GLSKGCFGLKLDRI GSM SGLRC	(SEQ ID NO: 1092)
	GLSKGCXFGLKLDRI GSM SGLGC	(SEQ ID NO: 1093)

(X: D-Phe)

(X: 3-amino-2-phenylpropionic acid)

(X: Cit)

(X: [CH₂NH]bond)

FIG. 28D

(X: N-Me-Phe)	GLSKGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1094)
(X: t-Bu-Gly)	GLSKGCFXLKLDRI GSM SGLGC	(SEQ ID NO: 1095)
(X: NHCH ₂ CH (Ph) CO)	GLSKGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1096)
	GQPREPQVYTLPPSGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1097)
	GERAFKAWAVARLSQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1098)
	GQHKDDNPNLPRGANPRGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1099)
	GHHSEQHHPHGANQQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1100)
	GAHHPHEHDTHGANKQQGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1101)
	FGIPMDRIGRNPRGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1102)
	GKRTGQYKLGSKTGP GPKGLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1103)
	SPKMVQSGGCFGLKLDRI GSM SGLGCKVLRH	(SEQ ID NO: 1104)
	GQPREPQVYTGANKQQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1105)
	GVPQVSTGTGANQQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1106)
	GQPSSSQSTGANQQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1107)
	GSTGQWHSESGANKQQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1108)
	GQTHSSGTQSGANKQQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1109)
	GSSSSSSSSSGANKQQGLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1110)
(X ₁ : [CH ₂ NH] bond; X ₂ and X ₃ : N-Me-Leu)	GLSKGCX ₁ FGX ₂ KLDRI GSM SGLGC	(SEQ ID NO: 1111)
(X ₁ and X ₂ : N-Me-Leu)	GLSKGCFGX ₁ KLDRI GSM SGLGC	(SEQ ID NO: 1112)
(X ₁ , X ₂ , and X ₃ : N-Me-Leu)	GLSKGCFGX ₁ KX ₂ DRIGSM SGLGC	(SEQ ID NO: 1113)
(X ₁ and X ₂ : N-Me-Leu)	GLSKGCFGX ₁ KX ₂ DRIGSM SGLGC	(SEQ ID NO: 1114)
	GLSRGCYGLKLDRI GSM SGLGC	(SEQ ID NO: 1115)
	GLSRGCFVLKLDRI GSM SGLGC	(SEQ ID NO: 1116)
	GLSRGCFSLKLDRI GSM SGLGC	(SEQ ID NO: 1117)
	GLSRGCFTLKLDRI GSM SGLGC	(SEQ ID NO: 1118)
	GLSRGCFGTKLDRI GSM SGLGC	(SEQ ID NO: 1119)
	GLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1120)
(X: Cit)	GLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1121)
	GLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1122)
	GLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1123)
(X: t-Bu-Ala)	GLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1124)

FIG. 28E

(X: pentanoic acid)	ELSEGCFLKLDRI GSM SGLGC	(SEQ ID NO: 1125)
(X: heptanoic acid)	XELSEGCFLKLDRI GSM SGLGC	(SEQ ID NO: 1126)
(X: pentanoic acid)	XELSEGCFLKLDRI GSM SGLGC	(SEQ ID NO: 1127)
(X: heptanoic acid)	XELSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1128)
(X: Cit)	XELSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1129)
	GLSKGCFGLXLDRI GSM SGLGC	(SEQ ID NO: 1130)
	GLSKGCFGLQLDRI GSM SGLGC	(SEQ ID NO: 1131)
	GLSKGCFGLRLDRI GSM SGLGC	(SEQ ID NO: 1132)
	GLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1133)
	GLSKGCFGLKLDRI SSMSGLGC	(SEQ ID NO: 1134)
(all D-amino acids)	GLSKGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1135)
(X: N-Me-Leu)	GLSKGCFGXKLDRI GSM SGLGC	(SEQ ID NO: 1136)
(X: N-Me-Leu)	GLSKGCFGLKXLDRI GSM SGLGC	(SEQ ID NO: 1137)
(X: N-Me-Leu)	GLSKGCFGLKLDRI GSM SGXGC	(SEQ ID NO: 1138)
(X: 3,4-dichloro-Phe)	GLSGGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1139)
(X: 3-Me-Phe)	GLSGGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1140)
	GLSRSCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1141)
	GLSRRCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1142)
	GLSGGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1143)
	GLSGGCFGLSLDRI GSM SGLGC	(SEQ ID NO: 1144)
	GLSRGCFGLKLDRI GQM SGLGC	(SEQ ID NO: 1145)
	GLSRGCFGLKLDRI GSM SGLGC	(SEQ ID NO: 1146)
	GLSRGCFGLKLDRI GSM SSLGC	(SEQ ID NO: 1147)
	GLSRGCFGLKLDRI GSM SRLGC	(SEQ ID NO: 1148)
	GLSRGCFGLKLDRI GSM SGRGC	(SEQ ID NO: 1149)
	GLSRGCFGLKLDRI GSM SGLSC	(SEQ ID NO: 1150)
	GLSRGCFGLKLDRI GSM SGLTC	(SEQ ID NO: 1151)
	GLSRGCFGLKLDRI GSM SGLRC	(SEQ ID NO: 1152)
(X: D-Phe)	GLSKGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1153)
(X: 3-Cl-Phe)	GLSKGCXGLKLDRI GSM SGLGC	(SEQ ID NO: 1154)
	RSSCFGGRI SRIGAC FFFF	(SEQ ID NO: 1155)

FIG. 30
CNP variants having Point Mutations at Position 17

CNP-X17	GLSKG CFGLKLD RIGSX SGLGC	(SEQ ID NO: 126)
CNP-F17	GLSKG CFGLKLD RIGSF SGLGC	(SEQ ID NO: 119)
CNP-L17	GLSKG CFGLKLD RIGSL SGLGC	(SEQ ID NO: 120)
CNP-I17	GLSKG CFGLKLD RIGSI SGLGC	(SEQ ID NO: 121)
CNP-T17	GLSKG CFGLKLD RIGST SGLGC	(SEQ ID NO: 122)
CNP-E17	GLSKG CFGLKLD RIGSE SGLGC	(SEQ ID NO: 156)
CNP-R17	GLSKG CFGLKLD RIGSR SGLGC	(SEQ ID NO: 157)
CNP-Y17	GLSKG CFGLKLD RIGSY SGLGC	(SEQ ID NO: 158)
CNP-C17	GLSKG CFGLKLD RIGSC SGLGC	(SEQ ID NO: 159)
CNP-P17	GLSKG CFGLKLD RIGSP SGLGC	(SEQ ID NO: 160)
CNP-D17	GLSKG CFGLKLD RIGSD SGLGC	(SEQ ID NO: 161)
CNP37-X17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSX SGLGC	(SEQ ID NO: 162)
CNP37-F17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSF SGLGC	(SEQ ID NO: 163)
CNP37-L17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSL SGLGC	(SEQ ID NO: 164)
CNP37-I17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSI SGLGC	(SEQ ID NO: 165)
CNP37-T17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGST SGLGC	(SEQ ID NO: 166)
CNP37-E17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSE SGLGC	(SEQ ID NO: 167)
CNP37-R17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSR SGLGC	(SEQ ID NO: 168)
CNP37-Y17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSY SGLGC	(SEQ ID NO: 169)
CNP37-C17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSC SGLGC	(SEQ ID NO: 170)
CNP37-P17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSP SGLGC	(SEQ ID NO: 171)
CNP37-D17	<i>QEHPN</i> ARKYKGANKKGLSKG CFGLKLD RIGSD SGLGC	(SEQ ID NO: 172)

FIG. 31A
Additional CNP variants having Point Mutations at Position 17

KA1-X17	<u>HGPQQEHHPN</u> ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC	(SEQ ID NO: 173)
KA2-X17	SGGGQEHHPN	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 174)
KA3-X17	GGGHGPQGEHHPN	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 175)
KA4-X17	GGSGGGQEHHPN	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 176)
KA5-X17	SGGGSGGGSGGGSGGGK	GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 177)
KA6-X17	<u>HGPQQEHHPN</u>	SGGGSGGGSGGGK GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 178)
KA7-X17	GGSGGGSGGGSGGGSGGGK	GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 179)
KA8-X17	GGGHGPQGS	GGGGSGGGSGGGK GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 180)
KB1-X17	<u>HKLRGQEHHPN</u>	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 181)
KB2-X17	GGGHKLRCQEHHPN	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 182)
KB3-X17	<u>HKLRGSGGGSGGGSGGGK</u>	GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 183)
KB4-X17	<u>GGGHKLRCGSGGGSGGGSGGGK</u>	GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 184)
PGCNP37-X17	<u>PGQEHHPN</u>	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 185)
KA1(E6)-X17	EEEEEEHGPQQEHHPN	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 186)
KA2(E6)-X17	EEEEEE	SGGGQEHHPN ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 187)
KA3(E6)-X17	EEEEEEGGGHGPQGEHHPN	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 188)
KA4(E6)-X17	EEEEEEGGSGGGQEHHPN	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 189)
KA5(E6)-X17	EEEEEE	SGGGSGGGSGGGSGGGK GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 190)
KA6(E6)-X17	EEEEEEHGPQQSGGGSGGGSGGGK	GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 191)
KA7(E6)-X17	EEEEEEGGSGGGSGGGSGGGSGGGK	GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 192)
KA8(E6)-X17	EEEEEEGGGHGPQGS	GGGGSGGGSGGGK GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 193)
KB1(E6)-X17	EEEEEEHKLRGQEHHPN	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 194)
KB2(E6)-X17	EEEEEEGGGHKLRCQEHHPN	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 195)
KB3(E6)-X17	EEEEEEHKLRGSGGGSGGGSGGGK	GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 196)
KB4(E6)-X17	EEEEEEGGGHKLRCGSGGGSGGGSGGGK	GANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 197)
E6PGCNP37-X17	EEEEEEPGQEHHPN	ARKYKGANKKGLSKGCFGLKLDRIGSXSLGC (SEQ ID NO: 198)

FIG. 31B
Additional CNP variants having Point Mutations at Position 17

C1 (E6) -X17	EEEEEESSGGGSGGGGGLSKG CFGLKLDRI GSX SLGC	(SEQ ID NO: 199)
C2 (E6) -X17	EEEEEEASTPANPQPAASSPGLSKG CFGLKLDRI GSX SLGC	(SEQ ID NO: 200)
C3 (E6) -X17	EEEEEEPSAAPQPNAPSTSAGLSKG CFGLKLDRI GSX SLGC	(SEQ ID NO: 201)
C4 (E6) -X17	EEEEEESSGGGSGGGKGAN KKGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 202)
C5 (E6) -X17	EEEEEESSGGGSGGGQGAN QQGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 203)
C6 (E6) -X17	EEEEEESSGGGSGGGKGAN KQGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 204)
C7 (E6) -X17	EEEEEESSGGGSGGGKGAN QKGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 205)
C8 (E6) -X17	EEEEEESSGGGSGGGQGAN KKGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 206)
C9 (E6) -X17	EEEEEESSGGGSGGGKGAN QQGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 207)
C10 (E6) -X17	EEEEEESSGGGSGGGQGAN KGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 208)
C11 (E6) -X17	EEEEEESSGGGSGGGQGAN KQGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 209)
D6CNP37-X17	DDDDDDQEHPNARKYKGAN KKGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 210)
C1 (D6) -X17	DDDDDDSSGGGSGGGGGLSKG CFGLKLDRI GSX SLGC	(SEQ ID NO: 211)
C2 (D6) -X17	DDDDDDASTPANPQPAASSGGLSKG CFGLKLDRI GSX SLGC	(SEQ ID NO: 212)
C3 (D6) -X17	DDDDDDGSSAAPQPNAPSTSAGLSKG CFGLKLDRI GSX SLGC	(SEQ ID NO: 213)
C4 (D6) -X17	DDDDDDSSGGGSGGGKGAN KKGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 214)
C5 (D6) -X17	DDDDDDSSGGGSGGGQGAN QGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 215)
C6 (D6) -X17	DDDDDDSSGGGSGGGKGAN KGLSKGCFGLKLDRI GSX SLGC	(SEQ ID NO: 216)
D6-14AAlinker-CNP-X17	DDDDDDSSGGGSGGGGGLSKG CFGLKLDRI GSX SLGC	(SEQ ID NO: 217)
CNP-14AAlinker-D6-X17	GLSKG CFGLKLDRI GSX SLGC GGGGSGGGGDDDD	(SEQ ID NO: 218)
CNP-Nterm1-X17	GSSAAPRPNAPSTSAGLSKG CFGLKLDRI GSX SLGC	(SEQ ID NO: 219)
CNP-Nterm2-X17	ASTSPANRPRAASSGGLSKG CFGLKLDRI GSX SLGC	(SEQ ID NO: 220)

FIG. 32
CNP variants having M17L

KA1 (E6) -L17	EEEEEEHGPQGEHPNARKYKGANKKKGLSKG CFGLKLDRI GSLSGLGC	(SEQ ID NO: 221)
KA2 (E6) -L17	EEEEEESSGGGQGEHPNARKYKGANKKKGLSKG CFGLKLDRI GSLSGLGC	(SEQ ID NO: 222)
KA3 (E6) -L17	EEEEEEGGGHGPQGEHPNARKYKGANKKKGLSKG CFGLKLDRI GSLSGLGC	(SEQ ID NO: 223)
KA4 (E6) -L17	EEEEEEGGSGGGQGEHPNARKYKGANKKKGLSKG CFGLKLDRI GSLSGLGC	(SEQ ID NO: 224)
KA5 (E6) -L17	EEEEEESSGGSGGGGSGGGKGAN CFGLKLDRI GSLSGLGC	(SEQ ID NO: 225)
KA6 (E6) -L17	EEEEEEHGPQSGGGSGGGKGAN CFGLKLDRI GSLSGLGC	(SEQ ID NO: 226)
KA7 (E6) -L17	EEEEEEGGSGGGSGGGSGGGKGAN CFGLKLDRI GSLSGLGC	(SEQ ID NO: 227)
KA8 (E6) -L17	EEEEEEGGGHGPQSGGGSGGGKGAN CFGLKLDRI GSLSGLGC	(SEQ ID NO: 228)
KB1 (E6) -L17	EEEEEEHKLRGQGEHPNARKYKGANKKKGLSKG CFGLKLDRI GSLSGLGC	(SEQ ID NO: 229)
KB2 (E6) -L17	EEEEEEGGGHKLRGQGEHPNARKYKGANKKKGLSKG CFGLKLDRI GSLSGLGC	(SEQ ID NO: 230)
KB3 (E6) -L17	EEEEEEHKLRGSGGGSGGGKGAN CFGLKLDRI GSLSGLGC	(SEQ ID NO: 231)
KB4 (E6) -L17	EEEEEEGGCHKLRGSGGGSGGGKGAN CFGLKLDRI GSLSGLGC	(SEQ ID NO: 232)
E6PGCNP37-L17	EEEEEPGQGEHPNARKYKGANKKKGLSKG CFGLKLDRI GSLSGLGC	(SEQ ID NO: 233)

FIG. 33A

NC2st-X17 and NC2B-X17 Protein Sequences

NC2st-X17 (w/ sig. seq.)	MGVHECPAWLWLLLSLLSLWPGAYAA SWSH PQFEQSGGGGGENLYFQGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSH PKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSGDGSEFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGG
NC2st-X17 (w/o sig. seq.)	ASWSH PQFEQSGGGGGENLYFQGGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSH DPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ PREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDGSEFFLYSKLTVDKS RWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGGGLSKGCFGLKIDRIGSXSLGCG
NC2B-X17 (w/sig. seq.)	MGVHECPAWLWLLLSLLSLWPGAYADKTH TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSH EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG QPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDGSEFFLYSKLTVDK SRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGGGGGGGGGGLSKGCFGLKIDRIGSXSLGCG
NC2B-X17 (w/o sig. seq.)	DKTH TCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLT CLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDGSEFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQK SLSLSPGKGGGGGGGGGGGGGGGGLSKGCFGLKIDRIGSXSLGCG (SEQ ID NO: 530)

FIG. 33C
NC2-X17 Variants

NC2-KGANKK-X17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIGSXSLGCG
(SEQ ID NO: 537)

NC2-KGANKK-X17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQK
SLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIGSXSLGCG (SEQ ID NO: 538)

NC2-KGANQK-X17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIGSXSLGCG
(SEQ ID NO: 539)

NC2-KGANQK-X17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQK
SLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIGSXSLGCG (SEQ ID NO: 540)

NC2-CNP53mut2-X17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGGDLQVDTQSQAAWAQLLQEHFNAQQYKGANKKGLSKGC
FGLKLDRIGSXSLGCG (SEQ ID NO: 541)

NC2-CNP53mut2-X17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQK
SLSLSPGKGGGDLQVDTQSQAAWAQLLQEHFNAQQYKGANKKGLSKGCFGLKLDRIGSXSLGCG (SEQ ID
NO: 542)

FIG. 33D

Fc-CNP53-X17 Constructs

Fc-CNP53-X17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYITLPPSRREMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANKGLSKGC
EGLKLDRIGSXSGLGCS (SEQ ID NO: 543)

Fc-CNP53-X17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSRREMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQK
SLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANKGLSKGCGFLKLDRIGSXSGLGCS (SEQ ID
NO: 544)

Fc-CNP53-AA-X17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYITLPPSRREMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNHYTQKSLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANAAGLSKGC
EGLKLDRIGSXSGLGCS (SEQ ID NO: 545)

Fc-CNP53-AA-X17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSRREMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNHYTQK
SLSLSPGKGGGDLRVDTKSRAAWARLLQEHHPNARKYKGANAAGLSKGCGFLKLDRIGSXSGLGCS (SEQ ID
NO: 546)

FIG. 33E

Constructs Having N-terminal NP-X17 fused to C-terminal Fc Domain

CNP-X17-16AAlinker-Fc-His ₁₀ (NC1)	GLSKGCFGLKLDRIGSXSLGCGGGGGGGGGSGDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGKGGENLYFQGSHHHHHHHHH (SEQ ID NO: 547)
CNP-X17-6AAlinker-Fc-His ₁₀ (NC3)	GLSKGCFGLKLDRIGSXSLGCGGGGGSGDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGKGGENLYFQGSHHHHHHHHH (SEQ ID NO: 548)
CNP-X17-6AAlinker-Fc	GLSKGCFGLKLDRIGSXSLGCGGGGGSGDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 549)
CDNP-X17-Fc	GLSKGCFGLKLDRIGSXSLGCPSLRDRPNAPSTADKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 550)
CDNP-X17-saa-Fc	GLSKGCFGLKLDRIGSXSLGCPSSAAPRPNAPSTADKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 551)
CDNP-X17-sra-Fc	GLSKGCFGLKLDRIGSXSLGCPSSRAPRPNAPSTADKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 552)

FIG. 34A NC2 Variants

NC2-KGANKK
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIQMSGLGC
(SEQ ID NO: 511)

NC2-KGANKK
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIQMSGLGC (SEQ ID NO: 512)

NC2-KGANQK
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIQMSGLGC
(SEQ ID NO: 513)

NC2-KGANQK
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIQMSGLGC (SEQ ID NO: 514)

NC2-CNP53mut2
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKGC
FGLKLDRIQMSGLGC (SEQ ID NO: 515)

NC2-CNP53mut2
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKGCFGLKLDRIQMSGLGC (SEQ ID
NO: 516)

FIG. 34B
D10-NC2 Variants

D10-NC2-KGANKK
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSMGSLGC (SEQ ID NO: 553)

D10-NC2-KGANKK
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI GSMGSLGC (SEQ ID NO: 554)

D10-NC2-KGANQK
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSMGSLGC (SEQ ID NO: 555)

D10-NC2-KGANQK
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI GSMGSLGC (SEQ ID NO: 556)

D10-NC2-CNP53mut2
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYK
ANKKGLSKGCFGLKLDRI GSMGSLGC (SEQ ID NO: 557)

D10-NC2-CNP53mut2
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYKANGKGLSKGCFGLKLDRI GSMGSLG
C (SEQ ID NO: 558)

FIG. 34C
NC2-F17 Variants

NC2-KGANKK-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGSGGGGSKGANKKGLSKGCFGLKLDRIQSFSGLGC
(SEQ ID NO: 559)

NC2-KGANKK-F17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGSGGGGSKGANKKGLSKGCFGLKLDRIQSFSGLGC (SEQ ID NO: 560)

NC2-KGANQK-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGSGGGGSKGANQKGLSKGCFGLKLDRIQSFSGLGC
(SEQ ID NO: 561)

NC2-KGANQK-F17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGSGGGGSKGANQKGLSKGCFGLKLDRIQSFSGLGC (SEQ ID NO: 562)

NC2-CNP53mut2-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFCSCVMHEALHNNHYTQKSLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKG
FGLKLDRIQSFSGLGC (SEQ ID NO: 563)

NC2-CNP53mut2-F17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTSISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTQK
SLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKGCFGLKLDRIQSFSGLGC (SEQ ID
NO: 564)

FIG. 34D D10-NC2-F17 Variants

D10-NC2-KGANKK-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSFSGLG (SEQ ID NO: 565)

D10-NC2-KGANKK-F17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI (SEQ ID NO: 566)

D10-NC2-KGANQK-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSFSGLG (SEQ ID NO: 567)

D10-NC2-KGANQK-F17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI (SEQ ID NO: 568)

D10-NC2-CNP53mut2-F17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGDDLQVDTQSQAAWAQQLLEHPNAQQYK
ANKKGLSKGCFGLKLDRI (SEQ ID NO: 569)

D10-NC2-CNP53mut2-F17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGDDLQVDTQSQAAWAQQLLEHPNAQQYKANGKGLSKGCFGLKLDRI (SEQ ID NO: 570)

FIG. 34E
NC2-L17 Variants

NC2-KGANKK-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIIGLSGLGC
(SEQ ID NO: 571)

NC2-KGANKK-L17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIIGLSGLGC (SEQ ID NO: 572)

NC2-KGANQK-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIIGLSGLGC
(SEQ ID NO: 573)

NC2-KGANQK-L17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIIGLSGLGC (SEQ ID NO: 574)

NC2-CNP53mut2-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGDLQVDTQSQAAWAQLLQEHFNAQQYKGANKKGLSKGC
FGLKLDRIIGLSGLGC (SEQ ID NO: 575)

NC2-CNP53mut2-L17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGDLQVDTQSQAAWAQLLQEHFNAQQYKGANKKGLSKGCFGLKLDRIIGLSGLGC (SEQ ID
NO: 576)

FIG. 34F
D10-NC2-L17 Variants

D10-NC2-KGANKK-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSLSLGLGC (SEQ ID NO: 577)

D10-NC2-KGANKK-L17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI (SEQ ID NO: 578)

D10-NC2-KGANQK-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSLSLGLGC (SEQ ID NO: 579)

D10-NC2-KGANQK-L17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI (SEQ ID NO: 580)

D10-NC2-CNP53mut2-L17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYK
ANKKGLSKGCFGLKLDRI (SEQ ID NO: 581)

D10-NC2-CNP53mut2-L17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYKANGKGLSKGCFGLKLDRI (SEQ ID NO: 582)

FIG. 34G
NC2-R17 Variants

NC2-KGANKK-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIGSSLGCG
(SEQ ID NO: 583)

NC2-KGANKK-R17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIGSSLGCG (SEQ ID NO: 584)

NC2-KGANQK-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGSGKANQKGLSKGCFGLKLDRIGSSLGCG
(SEQ ID NO: 585)

NC2-KGANQK-R17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGGSGGSGKANKQKGLSKGCFGLKLDRIGSSLGCG (SEQ ID NO: 586)

NC2-CNP53mut2-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGDLQVDTSQAAWAQLLQEHPNAAQQYKGANKKGLSKG
FGLKLDRIGSRLGCG (SEQ ID NO: 587)

NC2-CNP53mut2-R17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGDLQVDTSQAAWAQLLQEHPNAAQQYKGANKKGLSKGCFGLKLDRIGSSLGCG (SEQ ID
NO: 588)

FIG. 34H D10-NC2-R17 Variants

D10-NC2-KGANKK-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTEQKSLSPGKGGGGSGGSGKANGKGLSKGCFGLKLDRI
GSRSLGCG (SEQ ID NO: 589)

D10-NC2-KGANKK-R17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMH
EALHNNHYTEQKSLSPGKGGGGSGGSGKANGKGLSKGCFGLKLDRI GSRSLGCG (SEQ ID NO: 590)

D10-NC2-KGANQK-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTEQKSLSPGKGGGGSGGSGKANGKGLSKGCFGLKLDRI
GSRSLGCG (SEQ ID NO: 591)

D10-NC2-KGANQK-R17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMH
EALHNNHYTEQKSLSPGKGGGGSGGSGKANGKGLSKGCFGLKLDRI GSRSLGCG (SEQ ID NO: 592)

D10-NC2-CNP53mut2-R17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVFCSCVMHEALHNNHYTEQKSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYKQ
ANKKGLSKGCFGLKLDRI GSRSLGCG (SEQ ID NO: 593)

D10-NC2-CNP53mut2-R17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMH
EALHNNHYTEQKSLSPGKGGDDLQVDIQSQAAWAQLLEHPNAQQYKANGKGLSKGCFGLKLDRI GSRSLG
C (SEQ ID NO: 594)

FIG. 34I
NC2-Y17 Variants

NC2-KGANKK-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIGSYSGLG
(SEQ ID NO: 595)

NC2-KGANKK-Y17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGGSGGSGKANKKGLSKGCFGLKLDRIGSYSGLG (SEQ ID NO: 596)

NC2-KGANQK-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGGSGGSGKANQKGLSKGCFGLKLDRIGSYSGLG
(SEQ ID NO: 597)

NC2-KGANQK-Y17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGGSGGSGKANQKGLSKGCFGLKLDRIGSYSGLG (SEQ ID NO: 598)

NC2-CNP53mut2-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLLSLWPGAYADKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKG
QPREPQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMEALHNHYTQKSLSLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKG
FGLKLDRIGSYSGLG (SEQ ID NO: 599)

NC2-CNP53mut2-Y17
(w/o sig. seq.)

DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREEMTKNQVSLT
CLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMEALHNHYTQK
SLSLSPGKGGGDLQVDTQSQAAWAQLLQEHHPNAQQYKGANKKGLSKGCFGLKLDRIGSYSGLG (SEQ ID
NO: 600)

FIG. 34J D10-NC2-Y17 Variants

D10-NC2-KGANKK-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSYSGLG (SEQ ID NO: 601)

D10-NC2-KGANKK-Y17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI (SEQ ID NO: 602)

D10-NC2-KGANQK-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI
GSYSGLG (SEQ ID NO: 603)

D10-NC2-KGANQK-Y17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGGGGGGSGKANGKGLSKGCFGLKLDRI (SEQ ID NO: 604)

D10-NC2-CNP53mut2-Y17
(w/sig. seq.)

MGVHECPAWLWLLLSLSLWPGAYADDDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE
VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
IEKTIISKAKGQPRPEQVYITLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF
FLYSKLTVDKSRWQQGNVSCSVMHEALHNHYTQKSLSLSPGKGGDDLQVDTQSQAAWAQLLEHPNAQQYK
ANKKGLSKGCFGLKLDRI (SEQ ID NO: 605)

D10-NC2-CNP53mut2-Y17
(w/o sig. seq.)

DDDDDDDDDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE
VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP IEKTIISKAKGQPRPEQVYITLPPSRE
EMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSVMH
EALHNHYTQKSLSLSPGKGGDDLQVDTQSQAAWAQLLEHPNAQQYKANGKGLSKGCFGLKLDRI (SEQ ID NO: 606)